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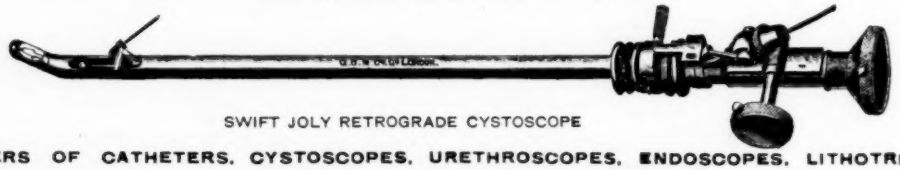

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The upper limit for the normal constant systolic pressure should never, whatever the age of the patient, be above 155 mm. of mercury. This figure is rather lower than used to be accepted, but is probably too high rather than too low. For the diastolic pressure a figure over 95 mm. is always to be considered as abnormal. There is no doubt, however, that remarkable temporary variations in systolic blood pressure may occur, especially under the stress of emotion, fear during examination, and the like, and it is common to find the first reading taken with the sphygmomanometer to be 10, 20, or even 30 mm. higher than subsequent readings.

In this connexion there is one important variation which can often be detected by the sphygmomanometer although the finger may do no more than suspect it. This is the pulsus alternans, which is particularly apt to be found in cases of high blood pressure and is shown by a doubling of the number of beats heard or felt below the arm-band, as the pressure is gradually lowered from the point at which the first sounds appear. The difference between the systolic pressures of alternate beats may be as much as 10 or even 15 mm. of mercury, and such a finding is always of the gravest importance.

The diastolic pressure, which is at least as important as the systolic, shows less variation and should always be recorded with the systolic.

When a persistently raised blood pressure is found it may be hard to determine to what extent (if any) it is associated with definite involvement of the kidney. The exact height of the pressure is no indication of the presence or degree of renal damage. Nor is peripheral arterio-sclerosis by any means constantly present; indeed the hard tortuous arteries so commonly found, for example, in manual labourers are often to be seen in cases where the blood pressure is not raised at all.

Hypertension occurs in practice essentially in three forms: (*a*) as a condition sui generis without changes in the kidney; (*b*) associated with renal arterio-sclerosis (nephrosclerosis arterio-sclerotica); and (*c*) associated with, and probably secondary to, granular contracted kidney of the true inflammatory type. The first of these is called essential hypertension or hyperpiesia; the two latter forms we group together clinically as chronic interstitial nephritis. There are, however, important distinctions between the two members of this group, and since the prognosis is largely dependent upon their separation I propose to say something firstly about a few points in this differentiation, and secondly and more particularly about the early recognition of renal damage of which-ever type it may be.

Arterio-sclerotic Kidney.

Briefly stated, high blood pressure associated with arterio-sclerotic kidneys presents the following features. The systolic blood pressure is subject to fairly wide variations under different circumstances, and may fall considerably with rest in bed. The diastolic pressure is apt to be relatively low, and thus the range between systolic and diastolic is high—i.e., the pulse pressure may be 120 mm. or even more. The patients are most usually elderly, often 60 or over, and frequently nervous and excitable about themselves; their colour is good—that is to say, there is no anæmia. The retinæ show arterio-sclerotic changes, pinching of the veins, and silver-wire arteries, and sometimes hæmorrhages. The prognosis, with suitable treatment, is comparatively good and the cause of death is apt to be apoplexy or heart failure.

Secondarily Contracted Kidney.

The second type, in which the high blood pressure is apparently the result of primary nephritis, corresponds to the true "small white kidney" which follows a recognised or unrecognised acute nephritis. Here the systolic blood pressure is usually far more fixed and seldom varies more than 10 or 15 mm. though it tends to rise somewhat during the course of the day; it is not necessarily very high, but the diastolic pressure is, in comparison, often much raised. The patient is generally younger, perhaps 30 or 40 years of age, and is markedly anæmic. The anæmia is, indeed, such a striking feature that these cases are often described as white hypertension, in contrast to the former type which is called red hypertension. The anæmia is probably the result of a chronic toxæmia, and is so important in prognosis that it is probably correct to say that when the red cell count is 3 million or under the patient will not live longer than two years. In these cases death is commonly from uræmia and the prognosis is bad.

A Differential Test.

In the early stages both these types of patient present themselves, as a rule, as simple cases of high blood pressure, with or without symptoms attributable to this. Of the various symptoms I would mention especially "rheumatic" pains in the limbs, headache (especially occipital), vertigo (sometimes), and dyspepsia (often). Dyspnœa on exertion is particularly common in the arterio-sclerotic type, as also are "rheumatic" pains, whilst headache is especially frequent in the inflammatory type. The early symptoms, however, rarely indicate the extent or nature of the renal damage; polyuria may not be complained of and in both types the urine may not be characteristic in its content of albumin, blood, or casts—all of which may indeed be absent.

It is in the diagnosis of the presence, degree, and to some extent of the type of nephritis in cases of this kind that I would like to call attention to one simple test which, though in no sense new, is yet recent in its application. I refer to the water test of kidney function of F. Volhard and Koranyi. This test is in routine use in almost all continental clinics, and widely in America, and I think it deserves more general recognition in this country. Thanks to the kindness of Prof. F. Langmead I have had the opportunity of applying it on many patients in the wards, and I feel that in such cases as I am discussing its simplicity and usefulness make it of very great value. The test, as I apply it, is as follows.

The patient is instructed to take as little fluid as possible from lunch-time onward, but to eat his ordinary diet; no fluids at all are drunk after 9 P.M. when the bladder is emptied (and the urine discarded). All the urine passed from this hour until 9 A.M. is then collected and measured, and a specimen is saved. At 9 A.M. a pint and a half of weak tea or water is drunk, and the urine is passed hourly for at least four, and if possible six, hours; each hourly specimen is measured and a sample is saved. The test can easily be carried out at home, preferably perhaps over a Saturday and Sunday, and if the hourly collection of specimens is difficult almost as much information may be obtained by examination of two-hourly samples. The specimens are all investigated as regards their volume and specific gravity.

The patient should be in bed during the test, for otherwise extrarenal factors—especially cardiac—are involved which lessen the value of the results. Such conditions as obvious heart failure, gross œdema, or severe diarrhœa, must naturally also vitiate the test, though they will not often be encountered in the type of patient that I am discussing. It is advisable, further, to carry out the test on one or two separate occasions if possible rather than to rely entirely upon one examination.

Night Urine.—The normal patient should not excrete more than about 20 oz. of urine during the night period, and the specific gravity should not be less than 1025. The restriction of fluids before going to bed ensures a maximum concentration in this specimen which normally bears a ratio to the day urine of about 1 to 3. The average volume in health is less than 15 oz., and the average specific gravity 1032 (**T.** Addis and M. C. Shevsky).

Water Test or Dilution Urine.—All the 30 oz. of fluid drunk in the morning should be excreted within 4½ to 5 hours; it is usually put out in not more than four. More than half—i.e., 15 oz.—should be excreted in the first two hours, and the rate of removal of the test dose is of great importance. The maximum flow should be during the second hour of the test, when the volume should not be less than 10 to 15 oz.; the flow at its maximum point reaches a rate of nearly half an ounce a minute (E. B. Verney); the specific gravity should fall to 1003 or lower. These figures have been obtained over a large series of normal subjects, and may be taken as substantially correct.

Results of the Water Test in Cases of High Blood Pressure.—All are agreed that the earliest evidence of renal impairment is shown by a poor concentration of the night urine. This is especially true of the inflammatory group of cases, in the early stages of which the volume is high (greater than a pint and often two or three pints), and the specific gravity is low. In the arterio-sclerotic kidney these changes are less marked; here the volume at night is slightly increased but the specific gravity is less reduced. Thus, for example, the volume may be 25 oz. and the specific gravity 1018, whilst in the inflammatory kidney the volume may be 40 oz. and the specific gravity 1006. In the *late* stages of both conditions the nocturnal polyuria ceases—a sign, as it were, of "decompensation" of the kidney—but the specific gravity remains fixed at 1010. Thus a small night volume with a specific gravity not greater than 1012 suggests a very serious prognosis.

The output of the test dose is also an excellent guide to the extent of renal damage. In the very lightest degrees there may be an excessive output, so that an abnormally high volume may be passed in four hours—well above the 30 oz. originally given. But the significance of this is somewhat doubtful, and in general it may be said that the less the amount put out of the 30 oz. given the worse the prognosis; the more the specific gravity remains fixed at 1010, the smaller each hourly volume becomes, and the more each equals another in volume the more grave is the impairment. Equality in volume of the consecutive specimens is a sign of serious import but indicates less severe impairment than does great diminution in the hourly amounts.

To some extent the response to the test may, I think, differentiate the nature of the lesion. Thus the inflammatory kidney which acts normally at its maximal excreting power shows a constant polyuria (by day and especially by night) but fails to excrete the added dose of fluid. A typical result is the following, the patient being a man of 55 who was sent home from abroad as a case of peripheral neuritis, with a blood pressure 220 systolic and 135 diastolic.

Hour.	Volume.	Sp. gr.	Hour.	Volume.	Sp. gr.
1st	1½ oz.	1011	4th	1½ oz.	1011
2nd	1 ,, ...	1010	5th	2 ,, ...	1010
3rd	2 ,, ...	1010			

Total excretion in 5 hours—of 30 oz. given—8 oz.

This patient showed a maximum urea concentration of 2·1 per cent. and a blood-urea of 60 mg. per cent., and died six weeks later from uræmia—an outcome which might not have been expected from the results of the urea-concentration test or blood examination alone.

The arterio-sclerotic kidney retains more of its power of excreting water, and most of the fluid given is excreted within six hours; the specific gravity is also lower and may fall in the largest specimen to 1005 or under. The following are two further examples of actual results which I think will demonstrate the value of the test.

A patient, aged 68, of high colour, had some arterio-sclerosis of the peripheral vessels. The blood pressure was 180/125, and there was a history of transitory left-sided hemiplegia. The maximum concentration of urea in the urine after 15 g. of urea was 3 per cent., but the minimum was down to 1·2, so that a range of 1·8 was found, which did not suggest any nitrogen retention in the blood; the blood-urea was in fact 20 mg. per 100 c.cm. There was slight albuminuria but no casts were found. The water test gave the following figures:—

Night urine.—Specific gravity 1015. Volume 23 oz.

Hourly specimens after 30 oz. of fluid—

Hour.	Volume.	Sp. gr.	Hour.	Volume.	Sp. gr.
1st	No urine ..	—	5th	1 oz.	1006
2nd	8 oz.	1014	6th	2 ,, ...	1012
3rd	4 ,, ...	1008	7th	2 ,, ...	1014
4th	4 ,, ...	1007			

In this case there is a delay with a moderate retention (11 oz.) at six hours; the specific gravity falls to 1006, giving a total range of 9. There is thus a definite picture of moderate arterio-sclerotic nephritis.

The second case, in contrast to the above, is that of a woman, aged 55, with some traces of albumin in the urine and a blood pressure of 175/110. The urea concentration was 4·2 per cent. after 15 g. of urea and in the dilute specimen 0·25 per cent.—i.e., there was a range of 3·95. The night urine showed a specific gravity of 1019 and volume 14 oz. The blood-urea was 26 mg. per 100 c.cm. The water test showed:—

Hour.	Volume.	Sp. gr.	Hour.	Volume.	Sp. gr.
1st	5 oz.	1010	3rd	5 oz.	1008
2nd	23 ,, ...	1003	4th	2 ,, ...	1012

Here the total volume of fluid is fully excreted in four hours and the range of specific gravity is high from 1019 to 1003—i.e., 16. This was therefore clearly a case in which a serious renal involvement could be confidently excluded, the only suspicious features being a slight failure of specific gravity in the night specimen and a somewhat excessive output of fluid in the second hour, with a total excretion just above the test quantity given. It will be seen that the volume and specific gravity tests alone were able to eliminate with some certainty any marked degree of arterio-sclerotic nephritis.

The main value of the test lies in estimating the extent of renal damage and is of the greatest value in prognosis. Thus if the specific gravity does not vary appreciably from 1010, and not more than half the test dose is excreted in six hours, the patient is unlikely to live more than a few months. To sum up, I will repeat the main points in estimating the degree of renal impairment.

Early Stages.—(1) A night urine of volume greater than 20 oz. and specific gravity below 1020. (2) Delayed and incomplete excretion of the test dose of water.

Later Stages.—(3) An increasingly smaller difference between maximum and minimum specific gravities, with a night urine of less volume but specific gravity approximately 1010; an equality in volume of the specimens following the fluid, the quantity of each being not more than 2 or 3 oz. (4) Fixation of specific gravity in all specimens at between 1009 and 1012.

In the attempt to differentiate early arterio-sclerotic from early inflammatory cases, we may say that, broadly speaking, the inflammatory kidney shows a greater polyuria, especially nocturnal, a greater fixation of specific gravity, and a greater inability to excrete a test dose of fluid. The arterio-sclerotic kidney shows a more normal daily urine volume, less nocturnal secretion, a higher range of specific gravity between concentrated and dilute specimens, and better power of excreting an excess of fluids.

Nitrogen Retention.

It may be that these distinctions are largely those of the severity of the renal impairment, but in accurate diagnosis and prognosis they are of real importance. They are of especial value in cases of high blood pressure with early kidney damage such as I am discussing, since albuminuria may be slight or absent and a raised blood-urea is a late occurrence.

Further in this stage the urea-concentration test—as usually carried out—may not show any renal defect. Thus in both arterio-sclerotic and inflammatory nephritis the maximum urea concentration in the urine after a dose of 15 g. of urea may be 2 per cent. or over—i.e., within normal limits. If, however, the dilute specimens after the dose of fluid are examined the contracted kidney may show a concentration of 1·9 per cent., or even an unaltered percentage, whilst the arterio-sclerotic kidney shows a figure of, say, 1 per cent. or even less. In this way, as was suggested by Dr. E. G. B. Calvert, estimation of the urea in the night specimen and in the dilute specimen after the fluid will provide a range of urea-concentration test, which gives similar information to the range of specific gravity but is less simple of application.

There is one further point in this connexion—namely, the detection of the presence of nitrogen retention in the blood. Even in uræmia there is not *always* a raised blood-urea, but it is a laboratory finding of great importance. A high blood-urea may be generally inferred when the specific gravity range is less than 3, and the maximum figure about 1010, whilst if the specific gravity in any specimen falls below 1006 it is unlikely to be present. In terms of urea concentration, if the maximum concentration is 2 per cent. or less, and the minimum is not lower than 0·2 to 0·3 per cent. less, the blood-urea is almost sure to be raised. A rough check upon the blood itself is easily available, without recourse to exact laboratory methods, in a simple test devised by Weltmann. This requires the use of two reagents only and is performed as follows:—

Five c.cm. of blood are taken from a vein and an approximately equal volume of trichloracetic acid is added to it at once. The mixture is then shaken and filtered. To the clear filtrate 5 drops of Ehrlich's aldehyde are added—a reagent to which I shall refer later. If the blood-urea is raised above about 40 mg. per cent., which is the upper normal figure, a greeny-yellow colour develops, which is darker and more intense the higher the blood-urea. If no colour develops any appreciable degree of nitrogen retention can be confidently excluded.

This test is simple, sufficiently accurate, and of real value—for example, in cases of coma when uræmia is suspected as the cause.

Types of High Blood Pressure with Early Renal Involvement.

	Arterio-sclerotic.	*Inflammatory.*
Age.—	Over 40.	Often under 40.
History.—	Previous good health.	Previous acute nephritis; often chronic focal sepsis.
Appearance.—	Red; excitable.	Pale; lethargic.
Main symptoms.—	Dyspnœa; rheumatic pains; angina pectoris.	Headache; dyspepsia; often polyuria.
Blood pressure.—	Variable.	Fixed.
Blood.—	Sometimes plethora or polycythæmia.	Anæmia.
Ocular changes. —	Silver-wire arteries; pinching of veins; hæmorrhages. Later sometimes "fluffy" patches of exudate.	Similar, but with fan-shaped exudate round macula.
Urine.—	Albumin, blood, and casts may be present or absent in either type.	
Night urine.—	Volume about 20 oz. (max. concentration). Specific gravity about 1018.	Volume more than 20 oz. Specific gravity 1015 or less.
Max. urea concentration.—	Approx. 2% or more.	Approx. 2% or less.
Min. urea concentration.—	Approx. 1% or less.	Approx. 2%.
Urea range.—	Approx. 1% or more.	Approx. 0·2% or less.
Water test.—	Good dilution; delay in output, but little retention over 6 hours.	Bad dilution; volumes of specimens small; equal half or less of the fluid excreted in 6 hours.
Specific gravity range.—	Fairly good—e.g., 1018 to 1005.	Relatively fixed—e.g., 1015 to 1008.
Blood-urea.—	Not raised till late.	Often raised early.
Duration.—	Often many years.	Short—1 to 4 years.
Outcome. —	Apoplexy; cardiac failure; angina pectoris.	Uræmia: intercurrent disease; heart failure.

Further Guides to the Condition of the Kidney.

The above table shows very schematically the main features which may help in differentiating the early stages of arterio-sclerotic from those of inflammatory kidney; it must not be taken as in any sense a hard-and-fast classification, and is merely meant as a rough guide to which there must be many exceptions. It must be remembered, moreover, that it is possible that these types may be but different stages of one and the same disease, which is probably primarily a vascular one. Nevertheless definite pathological differences can be found post mortem, and in practice the distinction is not an unimportant one. For a full discussion of this point I would refer the reader to Dr. T. Izod Bennett's Goulstonian lectures of 1928.[1]

Diagnostic Significance of the Presence of Urobilin in the Urine.

Urobilin is a biliary derivative which may sometimes appear in the urine and is quite distinct from the true bile-pigments, bilirubin and biliverdin, which are present in the blood and urine in such conditions as obstructive jaundice, and are detected in the urine by the formation of a green ring with either strong nitric acid or (better) a dilute solution of iodine in potassium iodide. Under the term urobilin I include both this substance itself and its probable precursor, urobilinogen, since their occurrence and importance are clinically the same.

The mode of formation of urobilin is as follows. The bile-pigments, bilirubin and biliverdin, are formed from the hæmoglobin of the blood, secreted in the bile by the liver, and reach the intestine through the common bile-duct. In the intestine they undergo a change into urobilin (probably through bacterial action), some of which appears in the stools under the name of stercobilin. Most of it, however, is absorbed back into the blood, reaches the liver again, and is then reconverted into bilirubin. So a circulation of the bile-pigments takes place.

Clearly an excess of urobilin may be present in the blood for two main reasons: (1) an excess of pigments may be formed originally from the blood so that an excess will reach the intestine and thus an excess of urobilin will be absorbed from the gut. (2) The liver may fail to reconvert the normal amount of urobilin which reaches it after absorption from the intestine. This liver function of converting urobilin to bilirubin is one that is easily impaired and appears to suffer in disorders of the liver before its other functions are appreciably affected. Further, with a normal kidney a slight excess of urobilin in the blood leads to its excretion in the urine, where it may be readily detected. The test for its presence is by means of Ehrlich's aldehyde reagent.

This solution—whose full name is para-dimethyl-amino-benzaldehyde—is readily obtainable and keeps fairly well in a dark coloured bottle. About 20 drops are added to an inch or so of urine in a test-tube and the presence of urobilin is shown by the appearance of a bright red colour which is apparent immediately in the cold if large amounts are present, more slowly reaching its maximum in one to three minutes if the amounts are only moderate, and producing only a faint tint on warming if there are only traces.

A strongly positive result with this test is always pathological, but slight traces of urobilin may sometimes appear in the afternoon urine of healthy people. The significance of a positive result is twofold. Firstly, it occurs in conditions where an excess of blood is being broken down; and, secondly, in conditions where liver function is defective. It is thus a simple and valuable test for disorders of the liver and for those of blood destruction. As a rule it is readily possible to distinguish which factor is at work, though both may sometimes be combined. The commonest of the two is that of liver impairment, and the value of this test in two or three common types of liver disorder is undoubted.

Urobilinuria and Defective Function of the Liver.

In *cirrhosis of the liver* the test is usually strongly positive and with other evidence is of very real diagnostic assistance; it may be positive before

[1] THE LANCET, 1928, i., 741.

other tests of hepatic function—such as the lævulose and galactose tolerance tests—show signs of insufficiency. Urobilin has also been shown by many workers to be constantly present in the urine after acute alcoholic excess, and this has even been urged as a legal point in those difficult cases of "drunk-in-charge-of-a-car." Its presence is at least evidence of the temporary damage to the liver which may be produced by alcoholic intoxication.

Secondly, in *catarrhal jaundice*, which we now know to be mainly toxic and not obstructive in nature, the test is positive at a very early stage, considerably before the appearance of the true bile-pigments which give the tests with iodine or nitric acid.

Thirdly, in *heart failure*, the test may be helpful, for an early sign of decompensation is the appearance of urobilin in the urine due to slight congestion of the liver; this, as is well known, may often occur before obvious signs such as dyspnœa, cyanosis, and gross œdema supervene. The dyspepsia and mild abdominal discomfort of apparently compensated mitral cases are often due to slight hepatic engorgement, and in such patients considerable amounts of urobilin may be present in the urine.

There is, moreover, a further point in this connexion to which I should like to call attention. As I stated, a normal kidney will excrete urobilin when it is present in the blood in only very slight excess. In nephritis this power is lost. Urobilinuria is thus an important consideration in cases of frank heart failure due to renal disease; in, for example, the common type of patient of, say, 50 to 60, who is brought to hospital with sudden acute heart failure, severe dyspnœa, œdema, cyanosis, and often auricular fibrillation. The vessels may be thickened, but the blood pressure may have fallen very low; there is often advanced emphysema and bronchitis, and it is sometimes difficult to know if the condition is primarily one of high blood pressure with "renal heart failure," or is the result of chronic pulmonary disease, myocardial degeneration, or pre-existing valvular lesions. The condition of the urine may be almost diagnostic. The usual features of heart failure urine are, briefly, small volume, high specific gravity, great acidity, with generally the presence of a large excess of uric acid. In renal heart failure the specific gravity is not so high—always an extremely bad sign in decompensated hearts—and Ehrlich's aldehyde test is negative; in heart failure with congestion of the kidneys but no previous renal disease there is abundant urobilin in the urine and a red colour appears immediately with Ehrlich's reagent. Thus in heart failure a urine of low specific gravity which gives a negative reaction for urobilin is of very grave significance, and suggests great care in the administration of diuretics, particularly of the new mercurial types, such as novarsurol or salyrgan, or even the simpler drugs such as calomel itself.

Whilst speaking of the subject of the urine in heart failure, I may perhaps mention a test which has recently been introduced from America and has been highly spoken of in Vienna and elsewhere, though I cannot myself vouch for its accuracy. It may be put in the form of an aphorism and is simply this: "If the urine in heart failure remains acid to methyl-red in spite of treatment, the patient will not recover." A few drops of this indicator, which is readily to be had, are added to about 5 c.cm. of urine, and high acidity is shown by a permanent red colour, using a control of the untreated urine; when the acidity lessens the indicator gives only a yellow colour. Thus if the urine remains red to methyl-red in spite of treatment, the prognosis must be considered hopeless. I would commend this test as possibly useful, but it requires confirmation in a larger number of cases.

Urobilinuria in Hæmolytic Conditions.

Returning to the second uses of the test for urobilin in the urine, its value is more limited. It is positive in conditions of excessive hæmolysis or blood destruction, such as occurs in malaria, the most important of which is pernicious anæmia. Here, owing to the abnormal hæmolysis, a positive aldehyde reaction is almost constant, and this fact may be useful in the differential diagnosis of pernicious anæmia from, for instance, carcinoma of the stomach. There is often a lemon-yellow tint of the skin in both diseases; in both there are abdominal symptoms, and radiography and blood examinations are not always easily obtainable. In a case with these symptoms a positive urobilin test is highly suggestive of a hæmolytic anæmia, and demands a full blood count without delay.

In all forms of hæmolytic jaundice—of which pernicious anæmia is an example—large amounts of urobilin are present in the urine unless there is associated severe nephritis. In obstructive jaundice it is necessarily absent, since no bile can reach the intestine to be converted into urobilin. The test may thus distinguish between hæmolytic jaundice, in which it is positive but the iodine test is negative, and obstructive jaundice, in which it is negative but iodine shows the presence of unaltered bilirubin. In such conditions the van den Bergh reaction in the plasma may not always be decisive, and, moreover, possesses the great disadvantage that if the blood is not tested within at the most two to three hours after its withdrawal from the vein, the results are fallacious. It is thus futile to carry out this test on blood specimens delivered through the post.

Urobilin in Hæmorrhage.

In extensive internal hæmorrhage an excess of blood-pigment is absorbed into the blood, and large amounts of urobilin may be passed in the urine. The test is, therefore, used widely abroad in the differential diagnosis of such conditions as ruptured ectopic pregnancy, and has a particular value in the diagnosis of hæmorrhagic infarction. For example, in pulmonary infarction, which may often cause difficulty in diagnosis, the test becomes positive some six to eight hours after the infarction, and remains strongly positive during the first two or three days, while the bulk of the broken-down blood is being absorbed. The value of the test in this connexion is stressed by continental authorities, and I have myself watched the appearance and disappearance of urobilin in the urine in two such cases.

To sum up, Ehrlich's aldehyde reagent is a useful addition to the small list of urinary test substances which are required in practice, and with due appreciation of the causes that may lead to its appearance, the presence of urobilin in the urine is a valuable diagnostic sign. The reagent is also helpful, as I have mentioned, as giving a rough test for the detection of a raised urea-concentration in the blood, with which it gives a greeny-yellow colour to the otherwise colourless blood filtrate.

Biliary Drainage.

The next diagnostic aid of recent introduction that I want to describe is one which may perhaps be considered somewhat impracticable. It is the examination of the bile obtained by duodenal catheterisation. Although this procedure has not been widely taken up in this country, I feel that it has a considerable value. I have had the opportunity of carrying out such an examination in 51 cases so far, and would like briefly to mention a few points about its usage which I have mainly learnt from my own experience. The test demands a lot of patience—both from the physician and from the patient—but very little apparatus. For those who can afford the time necessary it is simple to carry out.

Technique of Duodenal Catheterisation.—An ordinary Einhorn fractional test-meal tube is used, which is about the diameter of No. 6 rubber catheter. This is swallowed by the patient (who should have fasted for at least eight hours) up to the first ring on the tube. There is rarely much difficulty in this and cocainisation of the throat is not advisable since sensation returns during the course of the test and may lead to serious retching at an inopportune moment.

The gastric contents are withdrawn and the stomach is washed out with a few syringefuls of distilled water. The tube is then pushed down to the second ring, a distance of 28 inches, and the patient is turned on to the right side with the buttocks raised by a pillow; this position aids the

passage of the tube through the pyloric sphincter. This may take place almost at once, and is shown by the aspiration of a small quantity of alkaline bile-stained fluid—the duodenal content. It may, on the other hand, take a long time—often up to two or three hours—and one American investigator has recorded waiting 14 days for the tube to pass the pylorus! If there is delay I have found the sipping of a few ounces of very hot water useful, and slight withdrawal and reinsertion of the tube may sometimes be necessary; twice I have used atropine gr. 1/150 subcutaneously with success to aid relaxation of the sphincter. In general, however, the tube will pass in about one-half to two hours—the average time taken in my cases being one and three-quarter hours.

When the end of the tube is thought to be in the duodenum, a syringeful of water is blown in and if the tube is correctly placed this is not usually withdrawable; if it is still in the stomach the fluid can be at once sucked back, generally with a quantity of mucus. Fifty c.cm. of a 30 per cent. solution of magnesium sulphate are then slowly injected down the tube and some air is forced down after it. I inject the solution at ordinary room temperature, since I have found that warming it is apt to lead to nausea and regurgitation of the tube out of the duodenum; the magnesium sulphate is not as a rule withdrawable. After this, aspiration is carried out at short intervals, and normally the first bile-flow occurs within one to ten minutes. This flow is due to a reflex action from the duodenal mucous membrane and with healthy liver and biliary passages presents the following features. It is almost immediate in onset, rapid, painless, and of about 80 to 120 c.cm. volume. It shows, moreover, a typical gradation. First is a light yellow fluid, then a thick, dark green or brown viscid fluid, and finally it is of a clear golden limpid honey colour. The variations in these three types of bile—which are sometimes called A, B, and C bile—are important. The total flow usually lasts some 15 to 30 minutes.

Deductions from the Test.

I will not enter into the controversial subject of the exact origin of the three types of bile, and will merely refer briefly to some of the points in their examination by which this test may be of assistance. As with the urine and renal function, so may the rate and mode of secretion of the bile give almost as much information as a detailed chemical analysis of its constituents.

Complete failure to obtain bile on two repeated occasions is strong evidence of a stone in the bile passages. In association with jaundice it is almost conclusive of mechanical obstruction. It may thus be helpful in the diagnosis, for example, of carcinoma of the head of the pancreas from severe catarrhal jaundice, which is not always accurately possible by clinical means, and blood, urine, and stool examinations alone. Failure to obtain concentrated bile (bile B) can, though I think rarely, occur with healthy liver and biliary passages, but it is very unusual in the absence of disease to fail to obtain any bile at all if the test is carefully carried out. At the same time in a certain number of cases the attempt may have to be abandoned without it being certain that no bile could be obtained, on account of technical failure generally due to a revolt on the part of patient! In eight of the cases I have examined I must admit to complete non-success on these grounds. Pain during the flow suggests stone and infection in the gall-bladder. A very slow secretion with delayed onset and scanty volume seems also to be found—and I have observed this myself—in cholecystitis with or without stone.

In laboratory examination of the bile, as of the urine, the microscopic findings are of great importance. The presence of pus cells in the concentrated bile, often with many epithelial cells, is typical of cholecystitis; cholesterol crystals are not commonly seen, and when present in fair number are very suggestive of stone. Calcium bilirubinate crystals, which are very fine needles often clumped together into irregular masses, do not have such definite significance, and are often present in apparently normal patients. A large amount of albumin is present with biliary infection, but may also occur with disorder of the liver apart from infection. The normal in my cases has been less than ½ part per 1000, and more than 1 part per 1000 is always pathological. The presence of urobilin is also abnormal, and is seen especially with impaired hepatic function. In my cases large amounts have been present in ten and traces in four.

Catheterisation and Cholecystography.

I have not attempted to go into any detail about this test because I do not feel that its results are at present definite enough to warrant its use as an absolutely general procedure. It requires some practice both in performance and in the interpretation of results. Undue claims have, I think, been made for biliary drainage, just as undue claims were made when the fractional test-meal was first introduced. It nevertheless offers a very real aid in the diagnosis of cholecystitis and cholelithiasis and should, I think, be always employed where the existence of these conditions is in doubt. Its results should be viewed in association with those of radiography of the gall-bladder—a means of diagnosis which is also open to certain fallacies. With the use of the dye methods introduced by Graham a great advance has been made, but the method is still far from perfect, and I should like to say a few words about why this is so.

The dye most commonly used is sodium tetraiodo-phenolphthalein, and is generally given by mouth; at St. Mary's Hospital we are using a preparation named shadowcol, distributed by Messrs. Kodak, which causes very little nausea or diarrhœa. After absorption from the intestine the dye is excreted by the liver into the bile, and reaches the gall-bladder by way of the cystic duct. In the gall-bladder water is absorbed and the dye becomes concentrated so that it is sufficiently opaque to give a shadow on a radiographic film. The densest shadow is thus seen when the patient is a normal subject, and there may be no shadow for one or more of the following reasons: (1) The dye is not sufficiently absorbed from the alimentary tract. (2) The liver is unable to excrete it efficiently. (3) The cystic duct is blocked and bile cannot reach the gall-bladder; or (4) the gall-bladder is incapable of concentrating its contents satisfactorily.

With so many factors involved it is clear why cholecystographic results are not correct in probably more than 50 to 60 per cent. of cases examined. In association with results of biliary drainage, however, they gain in importance, and I feel that a direct examination of the bile is likely to increase in value in the near future. As to its application to bacteriological investigations there is as yet hardly sufficient evidence to speak at all definitely, but it seems to be of real help in the investigation of latent focal sepsis in the gall-bladder. To sum up, I would say that it should always be used when possible in doubtful cases of gall-bladder disease, and would stress especially the importance in diagnosis of pain during the flow, of the rapidity, volume, and appearance of the bile, and of the presence of pus, epithelial cells, and cholesterol crystals in the centrifuged deposit.

INDIGESTION.

In conclusion I should like to say a few words about the differential diagnosis of some of the causes of indigestion, with particular regard to the so-called functional dyspepsias. The common type of patient, most usually a woman, who has abdominal symptoms suggestive of perhaps a gastric ulcer, but in whom we feel confident that a "neurosis" is the true cause, may present great difficulty in diagnosis. Often enough the general behaviour of the patient is characteristic and the pain is usually one that gets worse on going to bed, but never wakes her up once she has got to sleep; it is probably fairly true that "a neurosis never woke a patient." At the same time we often wish for physical signs or laboratory tests that can confirm our suspicions and exclude organic disease.

Of the physical signs of neurosis there is no one alone that can be of genuine assistance, and even a combination of many together can only increase the probability of a functional condition. Of these signs I may mention the exaggerated deep reflexes, brisk abdominals, absent palate

reflex, and the evidences of various stigmata of degeneration such as asymmetries and minor deformities. To these is often added a condition of excessive vasomotor irritability or dermographia, in which a wide red mark rapidly appears after quite gently stroking the skin with a blunt instrument. There is frequently a tachycardia and a low blood pressure which reacts abnormally to mild exertion. A further sign which is not commonly present in persons of "non-neurotic nature" is an absence of the corneal reflex, which is perhaps the most suggestive of all the multitudinous signs of "neurasthenia" that have been proposed.

All these signs, however, are notoriously unreliable and laboratory aids in investigating the case are of real importance. Of these I would especially mention the value of an examination of the stools for *occult blood*, the finding of which definitely excludes a functional condition. It is so readily detectable that it should be looked for in all cases in which the possibility of ulcer or growth arises. In peptic ulcer intermittent bleeding is very common, and in carcinoma of the stomach occult blood is seldom absent and often continuous.

The test is very easily carried out, and the patient need only exclude meat (and meat extractives such as soup), fish, and green vegetables for two days from his diet. The simplest and most reliable technique is that of Gregerson, with the aid of benzidin tablets (benzidin 0·025 g. and barium peroxide 0·2 g.) obtainable from any chemist. One tablet or powder is dissolved in 5 to 10 c.cm. of strong acetic acid (50 per cent.), and a small particle of stool is rubbed up on the end of a match with a few drops of this solution. A positive result is shown by a green to deep blue colour appearing at once or within one to two minutes.

The use of these powders not only simplifies the test considerably, but excludes some of the fallacies of other methods of detecting occult blood. Indeed, A. G. Ogilvie considers that a blue colour obtained within 30 seconds is proof of occult blood in the stools entirely irrespective of the patient's previous diet. I realise that the test is well known, but I think it deserves more frequent application in general practice.

Test-meal analyses are, I am afraid, seldom of great assistance except in carcinoma of the stomach, pernicious anæmia, and duodenal ulcer. In the reflex and toxic dyspepsias of pulmonary tuberculosis, gall-bladder disease, renal disease, or chronic appendicitis, for example, the variations in gastric secretions are so diversely reported that assessment of their true significance is extremely difficult. In functional dyspepsia all types of test-meal results may be obtained.

There is one further test, which is old in origin but recent in its general utilisation, which may be employed with advantage in such cases—namely, the *red cell sedimentation test*. In spite of all that has been written and claimed for this test, especially in relation to pulmonary tuberculosis, the evidence of recent years shows that its real and great practical value lies simply in the differentiation of organic disease from functional disorder. It is in no way specific for any one form of disease, although exaggerated claims have often been made in this respect. It is a test that determines merely the rate at which the red cells fall to the bottom in citrated blood, and even now, in spite of the immense amount of work that has been done upon it, we do not know the exact factors that control this rate of sedimentation. Four volumes of blood are mixed with one volume of 3·8 per cent. sodium citrate and the rate of sinking of the red cells in this dilution is normally slow. I will not describe the exact details of the test, the results of which are recorded either in terms of the time taken for the cells to reach a given height in a standard tube (Westergren-Fahraeus) or of the height reached at a given interval of time (Linzenmeier).

In organic disease, especially where any form of tissue destruction is occurring, the rate of sedimentation is considerably increased. It has now been completely demonstrated that in a given case rapid sinking of the red cells above the normal rate excludes the diagnosis of a purely functional disorder.* A normal rate is unfortunately by no means such certain evidence of the *absence* of organic disease. In suspected gastric neurosis or other functional disorders, therefore, a normal sedimentation rate is confirmatory only of the diagnosis, whilst on the other hand a rapid sedimentation must make us immediately turn to an organic cause for the symptoms concerned. In this somewhat limited field of usefulness this simple and inexpensive test has, I think, a definite value. The details may be found in any recent text-book.

* A rapid sedimentation is normal during the early months of pregnancy.

SYPHILIS OF THE LUNG WITH PULMONARY ARTERITIS (AYERZA'S DISEASE).

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With a Report upon the Pathological Findings by
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MORE than a hundred years ago Laënnec described dilatation of the pulmonary artery in chronic affections of the lungs.[1] Andral, in 1829,[2] stated that most of the lesions which occur in the aorta are also to be found in the pulmonary artery, but much more rarely. Huchard, in 1893,[3] drew up a table of arteries showing their liability to atheroma. He quoted similar tables by Rokitansky and Lobstein confirming his conclusion that the pulmonary artery is, of all the large arteries in the body, one of the least liable to atheroma. Romberg, in 1891,[4] recorded a case of a man aged 24, in which there was extensive sclerosis throughout the pulmonary artery and its branches and hypertrophy of the right ventricle without apparent cause. Dyspnœa and cyanosis of the skin and mucous membranes were prominent symptoms for many months before death.

Sansom, in 1896,[5] working at the London Hospital, summarised the subject. He concluded that acute and subacute pulmonic endarteritis are mostly due to the extension of septic endocarditis, but that the inflammation may be due to syphilis. In discussing chronic, endarteritis and atheroma of the pulmonary artery he mentioned congenital defects, mitral stenosis, and obstructive diseases of the lung as important ætiological factors.

In 1901, Abel Ayerza, professor of medicine in the National University of Buenos Aires, drew attention in an unpublished clinical lecture to the morbid entity of "cardiacos negros," a syndrome which Escudero[6] claims to have shown in 1905 to be associated with generalised sclerosis of the pulmonary artery and hypertrophy of the right ventricle. Though these two workers had so far only confirmed Romberg's observations we find the term Ayerza's disease, which was used for the first time by Marty in 1909,[7] creeping into general use. Leonard Rogers, in 1909,[8] writing on nine Bengalis suffering from primary atheroma of the pulmonary artery accompanied by extreme right heart hypertrophy but without valvular lesions, concluded that the extensive atheroma of the whole of the pulmonary arteries was syphilitic in origin. The symptoms from which his patients suffered were palpitations, dyspnœa, and dropsy; he did not stress cyanosis. Escudero, however, in 1911,[6] revised his opinion of the pathological basis of "cardiacos negros" in that he now associated the sclerosis of the pulmonary artery with bronchial syphilis.

Advances in the diagnosis of lesions of the pulmonary artery were made by Possett in 1908[9] who emphasised the importance of radiological and electrocardiographic findings.

Arrillaga,[10] in 1913, in a monograph, the English translation of which was kindly lent to me by Dr. Geoffrey Evans, gave a detailed account of "cardiacos negros." His main conclusions were as follows:—

1. The ætiological factors of "cardiacos negros" are chronic pulmonary disease processes, asthma, chronic bronchitis, tuberculosis, and pleural adhesions—in short, all disturbances which have as their final result a state of pulmonary emphysema.

2. These processes evoke, in a pulmonary artery, rendered sensitive by slow infections such as syphilis, paludism, &c., or by intoxications, a sclerotic process which causes a physiological stenosis of the arterial tract which the blood follows on its way to oxygenation.

3. This sclerosis of the pulmonary artery can not only be demonstrated microscopically and histologically in the specimens obtained from these patients, but may also be recognised clinically in hæmoptysis, cyanosis, dyspnœa, and hypercyanotic angina, from which these patients suffer.

4. The right heart undergoes an enormous hypertrophy involving both the auricle and the ventricle which are forced to struggle against the obstacle in the peripheral circulation.

5. This hypertrophy, as well as the dilatation of the pulmonary artery in its early stages, can be clearly seen by radioscopy and radiophotography.

6. The principal symptoms of this entity are: cyanosis, polycythæmia, dyspnœa, cough with mucous or mucopurulent expectoration, cephalalgia, hypercyanotic angina, hæmoptysis, vertigo, an overpowering desire for sleep, &c.

7. The pulmonary stage is a very long one; after about 20 years as a pulmonary complaint it comes to the notice of the clinician in its cardiac phase.

8. The course of the "cardiacos negros" stage is also long and varies from two to five years.

9. Some of the patients may end as "cardiacos negros" and after showing the right gallop rhythm die in their sleep, without having suffered from a trace of œdema. Others, in whom degeneration of the cardiac fibre had taken place, early succumb to ordinary asystole caused by failure of the right heart and die in a state of advanced anasarca. Finally, some die of complications, of which the commonest is broncho-pneumonia.

In subsequent writings, Arrillaga[11 12] insists more positively that syphilis is the essential ætiological factor in the evolution of the "cardiacos negros" and that chronic cardiopulmonary diseases play only a subsidiary part.

Of recent years there have been many contributions, American and European, to the literature of sclerosis of the pulmonary artery. Warthin, in 1917,[13] demonstrated for the first time the *Spironema pallidum* in the wall of the pulmonary artery in a case of syphilitic arteritis and aneurysm of this vessel. Four years later Elizaldo confirmed this finding in one of Arrillaga's patients[14] who had a history of syphilis and a positive Wassermann reaction. M. Giroux, in 1910,[15] and Marcel Thomas, in 1927,[16] contributed detailed theses on lesions of the pulmonary artery. Cheney,[17] in the same year, reported two cases of Ayerza's disease, and concluded that the term should be restricted to cases of sclerosis of the pulmonary artery and hypertrophy of the right heart due to syphilis. Clarke, Coombs, Hadfield, and Todd[21] recently published details of five cases of congenital and acquired lesions of the pulmonary artery which had come to autopsy.

"*Primary*" *Sclerosis of the Pulmonary Artery.*

Though many authors have published cases of so-called primary sclerosis (non-syphilitic) of the pulmonary artery the existence of such an entity is in doubt.

Prof. H. M. Turnbull in his early[18] and later work upon the arteries has found thickening of the pulmonary arteries to be almost entirely intimal. The intimal thickenings are composed either of layers of muscle and elastic fibres, which have usually undergone a greater or less degeneration, or of granulation tissue, the endarteritis fibrosa of Jores.

In the formation of the layers of muscle and elastic fibres the elastic stripe separates from the elastic lamella and proliferates. Layers of muscle and elastic fibres of similar structure are normally developed in a similar manner during early years in the aorta and its large elastic branches. An increase in magnitude of the intimal layers of muscle and elastic fibres in these arteries and their development in other arteries can only be regarded as a hypertrophy. Hypertrophied intima is prone to degeneration, particularly in older subjects. Slight intimal hypertrophy is found in the pulmonary arteries of the elderly, and is doubtless due to medial degeneration; one or two minute flecks of atheroma can usually be detected on careful examination with the naked eye, and more extensive focal degeneration of the intima is found under the microscope. Greater degrees of intimal hypertrophy, with greater degeneration, are found in mitral stenosis and all other conditions causing an obstruction to the circulation in the lungs.

Far the commonest form of intimal degeneration in the pulmonary arteries is a degeneration that is superimposed upon hypertrophy and is independent of inflammation. From his experience of the aorta, however, Prof. Turnbull has no doubt that intimal degeneration may complicate chronic inflammation of the pulmonary stem and large branches, although he has not personally had an example. When syphilitic aortitis is confined to the adventitia and media, the overlying intima may hypertrophy and then undergo atheromatous degeneration. Usually the aortitis implicates the intima and causes a granulomatous thickening. When this inflammatory thickening has become sclerotic it usually becomes impregnated with calcium or undergoes true fatty and calcareous atheroma, just as calcareous impregnation and atheroma tend to affect cardiac valves which have been sclerosed by chronic inflammation. Such degenerations secondary to inflammation may doubtless, therefore, occur on the rare occasions when the pulmonary stem and large branches are affected by syphilitic inflammation. In syphilitic and tuberculous arteritis of the smaller pulmonary arteries, and the small arteries in other organs, he has not seen secondary degeneration.

Such intimal degeneration of the larger pulmonary arteries, although a secondary complication of syphilitic inflammation of these larger arteries, might be called primary, in so far as it is not secondary to obstruction within the lungs. Prof. Turnbull has not had an example of such degeneration of the intima of the pulmonary arteries superimposed upon syphilitic or tuberculous inflammation of the subjacent coats. His cases belong to the group in which there is no underlying inflammation. When, in his experience, there has been degenerative thickening of the intima of the pulmonary arteries, there has always been histological evidence of intimal hypertrophy having preceded the degeneration; when the hypertrophy and degeneration have been great, there has always been an obvious cause of obstruction to the pulmonary circulation. He has therefore found no evidence of a primary, non-inflammatory sclerosis of the pulmonary arteries, except the slight atherosclerosis of elderly subjects.

Definition of Ayerza's Disease.

There can be little doubt that many of the cases referred to by Arrillaga in his thesis[10] on "cardiacos negros" belonged to the already well-known group of chronic cardiopulmonary diseases producing right heart hypertrophy and later failure. Parkinson and Clark-Kennedy's paper on Heart Failure with Normal Rhythm[19] includes a series of such cases. Intimal hypertrophy and degeneration of the pulmonary arteries in such cases were also well known as secondary effects.

The clinical manifestations of such a sequence of events are cyanosis, dyspnœa, hæmoptysis, clubbing of the fingers, and secondary erythrocythæmia. The signs and symptoms of congestive heart failure are usually superadded before death.

Ayerza has left no written account of his observations, but if we are to accept his pupil Arrillaga's writings as embodying the teaching of his master, Ayerza's claim to a place in medical nosology must be based on his discovery of the "black cardiac"

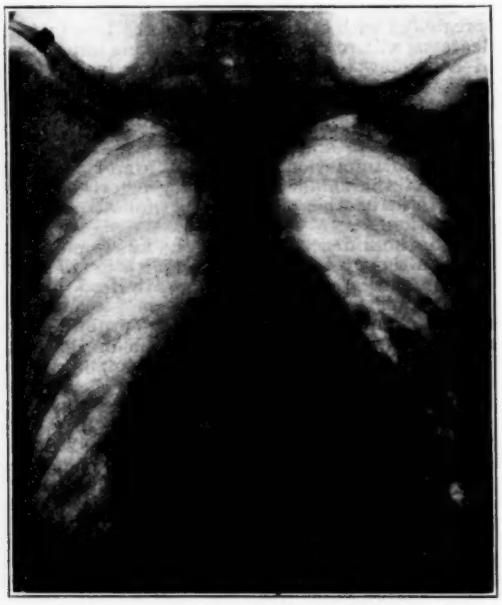
syndrome due to *syphilis* of the lung and pulmonary arteries. The many accurate macroscopic and microscopic descriptions of undoubted syphilitic pulmonary arteritis, confirmed by Warthin and Elizaldo's demonstration of the *Spironema pallidum* in the wall of such arteries, have placed the existence of this entity on a sound footing. Now just as emphysema and non-specific fibrosis of the lungs may, by causing obstruction and hypertension in the lesser circulation, induce intimal hypertrophy and degeneration of the pulmonary artery so also can peribronchial and interstitial pulmonary syphilis induce these changes.

In the case here reported the smaller branches are the seat of obliterating syphilitic arteritis, whereas the pulmonary stem and main branches show the changes due to hypertension—namely, intimal hypertrophy with superimposed atheromatous degeneration.

Clinical Features.

Both sexes are affected about equally, there being 15 men out of 27 cases collected from the literature by Cheney. He says that cases have been recorded in Europe, South America, United States, and India. The patient usually does not present himself with

FIG. 1.



Antero-posterior radiogram of chest. The enlarged globular shadow of the heart is seen. On its left border the prominence immediately below the small aortic knuckle is the pulmonary artery which is larger and denser than normal; the mottling in the lower lung-fields is due to fibrosis and congestion.

typical symptoms until he has reached the age-period 20–50 years. Cough and expectoration may have been present for many years. Gradually dyspnœa, cyanosis, persistent headache, and drowsiness become added to the picture. Orthopnœa is the rule, and hæmoptysis is common. Oppression in the chest, particularly after exertion, may be a prominent symptom. The somnolence often considerably mitigates the patient's sufferings and may be partly responsible for prolonging the life of the patient after extreme cyanosis has developed. Congestive heart failure more frequently than not supervenes before death. The cardiaco negro may die, however, in his sleep without manifesting any of the signs or symptoms of heart failure.

Though the average case runs a protracted course over many years, others such as ours die within two years of their first symptom.

On examination the temperature is often subnormal; the pulse and respiration-rate may be 100 and 30 respectively. Cyanosis of the head and neck, mucous membranes, conjunctivæ, and periphery of the limbs is a striking feature even when the patient is at rest; that of the buccal mucosa often extends to the soft palate and posterior pharyngeal wall. The pulse is regular, and the palpable arteries are not unusually thickened. Clubbing of the fingers is usually seen. The blood pressure is within normal limits. Cardiac and hepatic dullness may be encroached upon by lung resonance; the heart sounds will then be distant. Unless emphysema is too great systolic pulsation in the pulmonary artery can be seen and palpated, and the pulmonary second sound is accentuated.

Five to fifteen ounces of muco-purulent sputum may be expectorated daily. The accessory muscles of respiration, particularly the scalenes, hold the barrel-shaped chest in the position of full inspiration. Lung resonance is increased and on auscultation loss of vesicular murmur and prolonged expiration is heard. Rhonchi and crepitations are heard at the bases.

General anasarca and hepatic enlargement depend on whether congestive heart failure has occurred or not. Blood examination shows a red count of between five and ten million, the hæmoglobin being above normal and the colour-index below 1.

Radiological Examination.

1. The heart shadow is much enlarged both to the right and to the left, giving a globular appearance. 2. The enlarged pulmonary artery is seen vigorously pulsating below the aortic knuckle, which seems small by comparison. A half turn of the patient to the left (first oblique position) gives an even better idea of the size of the pulmonary artery, which may even reach aneurysmal proportions.[20] Each pulsation will be seen to follow immediately upon ventricular systole. 3. The shadows of both lung roots are abnormally large and dense and the component arteries may visibly pulsate; shadows radiating from them into the lung parenchyma may be due to vascular engorgement or to fibrosis. 4. Evidences of emphysema may be found, such as horizontal position of the clavicles and ribs, wide intercostal spaces, and low position of the diaphragm with diminished movement. An electrocardiogram will show striking right ventricular predominance.

Differential Diagnosis.

Any disease process leading to pulmonary hypertension may produce symptoms clinically indistinguishable from Ayerza's disease. Chronic disease of the lung and pleura, chronic valvular lesions of the heart, particularly mitral stenosis, congenital morbus cordis, malformations of the pulmonary artery, thoracic deformities should all be excluded before the diagnosis is suggested.

Difficulty may arise in differentiating other causes of cyanosis, especially erythræmia (Vaquez-Osler disease). Reliance must be placed on the clinical, radiographic, and electrocardiographic evidence of dilatation and hypertrophy of the right ventricle and pulmonary artery together with evidence of syphilis in those exhibiting Ayerza's syndrome. The spleen is not usually palpable and the blood pressure is normal. Blood counts may be identical in the two conditions.

Enlarged mediastinal glands, thoracic tumours, and aortic aneurysms may, by obstructing the superior vena cava, cause congestion and cyanosis of the head and neck. The limited distribution of the cyanosis, the enlargement of the superficial collateral circulation, and radiographic examination make the diagnosis easy. Mediastinal tumours and aneurysms, however, by pressing on the pulmonary artery may cause difficulty. Congenital morbus cordis, even when unassociated with marked abnormality of the pulmonary artery, may be the cause of extreme cyanosis. It should also be borne in mind that aneurysm of the pulmonary artery may occur as a congenital abnormality; Bedford [20] reports an

example of this complicated by infective endocarditis.

Treatment.

Prophylaxis and treatment whilst the disease is in its pulmonary stage offer the best chances of success. Once cyanosis has become established little can be done apart from symptomatic treatment. Even if the Wassermann reaction is negative anti-syphilitic remedies should be given if there is a positive history or if there are signs of old visceral or cutaneous lesions. In the presence of persistent headache or frequently recurring hæmoptyses venesection should be employed. Oxygen administered by the intranasal method and other measures usual in cardiac failure from other causes may help.

FIG. 2.

Section through the left lung. The larger pulmonary arteries are greatly dilated and have thickened walls. The lower lobe is seen to extend almost as far as the apex of the lung and largely replaces the shrunken fibrotic upper lobe, which has retracted inwards. Inferiorly many dilated and thick-walled bronchioles lie closely packed together; around these a reticular fibrosis is clearly shown.

Illustrative Case.

A.B., a male nurse, aged 45, was admitted to the London Hospital with a history of 18 months' increasing dyspnœa which was worse on exertion. Five months previously he had had two small hæmoptyses, the sputum being only tinged with blood. A month later he noticed that his lips were blue and that his feet became swollen after exercise. Cough was never a prominent symptom.

Past History.—31 years before he had had typhoid fever, and 25 years before he had had ulcers on the soft palate, which left two small perforations.

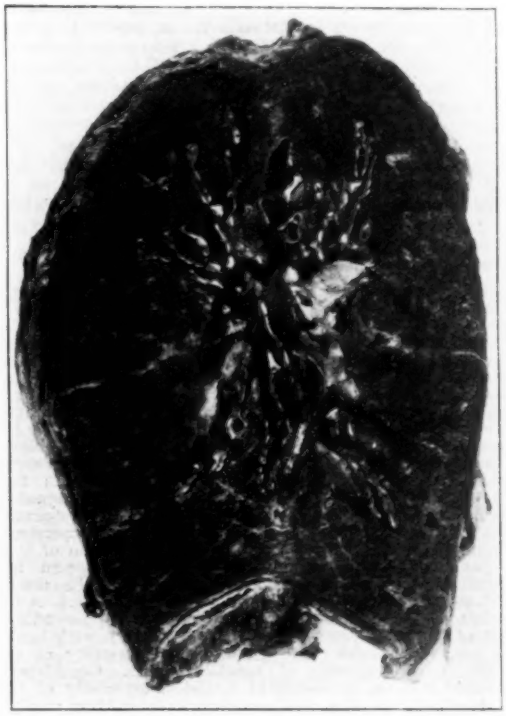
On Examination.—Cyanosis of lips, ears, cheeks, and feet. Orthopnœa present. Considerable œdema of the feet, legs, thighs, and lumbar region. Extensive tattoo marks over trunk and limbs. Moderate clubbing of the fingers, and cyanosis of the nail-beds. Two small perforations of the soft palate slightly to the left of the mid-line and close to the junction of the hard and soft palate. Small white scar on under surface of glans penis.

Circulatory System.—Pulse 100, regular, and of moderate volume. Blood pressure 120–180. Brachial and radial arteries not thickened. Apex-beat not defined, left border of cardiac dullness one inch external to the left nipple line. Heart sounds normal.

Respiratory System.—Sputum, three ounces of muco-purulent sputum daily. Chest held in position of full inspiration. Scalene muscles in action during inspiration. Inspiration everwhere harsh and expiration prolonged. Coarse crepitations at both bases, more numerous on the left side.

Abdomen slightly distended, lower border of liver palpable two fingers-breadth below the costal margin. No tenderness over the liver. Spleen and kidneys not palpable.

FIG. 3.



Section through the right lung. The dilated and thickened larger pulmonary arteries are seen in longitudinal and transverse section. A delicate reticular fibrosis is conspicuous in the greater part of both the upper and lower lobes. In the base larger fibrous trabeculæ and stellate patches of fibrosis are present in addition.

Nervous System.—Pupils equal, react to light and accommodation. Knee-jerks and ankle-jerks equal and active. Bilateral flexor plantar response.

Reports.—Urine free from albumin and sugar. Wassermann reaction *positive* in serum. Blood-urea, 0·034 per cent. White cell count, 7120. Polymorphonuclear leucocytes, 65 per cent., large hyaline cells 11·5 per cent., small lymphocytes, 20 per cent., large lymphocytes 3·5 per cent. By an oversight the total number of red blood corpuscles and the hæmoglobin value were not estimated.

Radiographic Examination (Dr. George Vilvandré).—Enlargement of the heart to the right and left, the cardiac shadow presenting a globular appearance. Left border of the heart ¾ in. external to the mid-clavicular line. Pulmonary artery unduly prominent, lying below the normal aortic knuckle (Fig. 1). Both lung roots obscured by the large cardiac shadow. General coarse mottling shown by the bases of lungs.

Electrocardiogram.—Right ventricular predominance. A negative "T" in leads II. and III. due possibly to digitalis.

Course.—Digitalis was given without benefit until coupling took place, a polygram showing alternate ventricular premature beats. Despite the administration also of diuretin, iodides, and mercury the œdema increased, and the amount of urine decreased from 60 to 8 ounces per diem. The pulse continued regular except for the above-mentioned digitalis coupling, and varied between 56 and 110 until just before death when it rose to 120. The patient died four weeks after

admission, the temperature remaining between 96 and 97° F. during the whole period.

This patient, admitted with cyanosis, severe though by no means black, with congestive heart failure, with œdema, yet with normal heart sounds, was at first regarded as a case of heart failure with normal rhythm, probably due to syphilis affecting the orifices of the coronary arteries (Wassermann reaction positive; perforated palate). The X ray appearance showing no aortic enlargement but prominence of the pulmonary artery shed doubt on the preliminary diagnosis and it was not until the necropsy that the exact nature of the underlying lesion was determined.

I am indebted to Dr. John Parkinson for his advice and for permission to publish the notes of this case, and to Dr. D. Evan Bedford for help with the bibliography, and to Prof. Hubert Turnbull for his remarks upon degeneration of the pulmonary arteries, and for his report upon the necropsy.

Report upon Pathological Findings.

By Hubert M. Turnbull.

Summary of necropsy (P.M. 446. 1928).—Failure of hypertrophied right heart. Syphilitic interstitial fibrosis of lungs and extensive endarteritis of pulmonary arteries.

Anthracosis and plasma-cell infiltration of bronchial glands. Conspicuous patchy atheroma of hypertrophied intima of pulmonary stem and of branches not affected by arteritis. Lumen of pulmonary stem, 8·5 cm. in circumference; wall, 0·1 cm. thick; lumen of ascending aorta, 7·5 cm. in circumference. Slight atheroma of arteries of greater circulation. Great hypertrophy and dilatation of right ventricle and auricle; slight atrophy of left ventricle. Foramen ovale closed. Milk spots on anterior surface of right ventricle and posterior surface of right auricle. Congestion and confluent central back-pressure atrophy of liver. Back-pressure spleen and kidneys. Great congestion of stomach; area (2·2 by 1·5 cm.) of purulent streptococcal inflammation and necrosis of centre of posterior wall of body of stomach. Area (2·5 by 1·1 by 1·3 cm.) of purulent hæmorrhagic inflammation and fat necrosis in subjacent portion of body of pancreas. Great submucous œdema of cæcum and ascending colon; œdema of bone marrow; general anasarca, greatest in feet, legs, and back; ascites (907·2 c.cm.). A few patches of fatty hæmatogenous marrow in upper half of shaft of femur. Perforation (0·4 by 0·15 cm.), with healed and scarred margins, through anterior extremity of soft palate. Great fibrosis of faucial tonsils. Considerable syphilitic fibrosis of bodies of testicles, especially of left. Faint, slightly sunken, white scar on under surface of glans penis. Colloid adenoma (0·6 cm. diam.) in lower pole of left lobe of thyroid. Thymus masked by fat. A few scars (of war wounds) on right buttock. Healed amputation of second toe of right foot. Superficial erosion of skin over buttocks. Wasted man.

Weights: Body, 64·27 kg. (length 1·72 metre); brain, 1318·3 g.; liver, 1234·0 g.; heart, 453·6 g.; kidneys, 368·7 g.; spleen, 212·6 g.; pancreas, 98·7 g.; thyroid, 20 g.; thymus, 14·2 g.; suprarenal bodies, 11·3 g.; pituitary body, 0·6 g.

Macroscopic Appearances.

The thickened parietal and visceral pleuræ were everywhere either completely fused or bound together by a net of fibrous sheets and trabeculæ. In places they could be torn apart so as to expose a visceral layer which was milky-white and either quite opaque or sufficiently translucent to show a background of dark slate. Cut surfaces of the lungs, except in the upper half of the posterior part of the left lower lobe and in the apex of the right lower lobe, had to the naked eye a conspicuously spongy appearance. A net of pearly fibrous tissue enclosed spaces, of which the larger were obviously dilated bronchioles and the smaller dilated vesicles. The fibrous septa of this sponge varied considerably in thickness in different places. Even the most delicate were clearly visible to the naked eye. Those bounding bronchioles were stouter than those bounding adjacent vesicles. Comparison of different areas showed that in general the stouter the septa were the larger were the pores. The sponge was traversed and interrupted by pearly branching trabeculæ about one millimetre broad and by pearly stellate patches about one centimetre in diameter. Some of these trabeculæ and patches could be seen to surround bronchi and large bronchioles; any bronchus or bronchiole which happened to be cut transversely in the centre of a patch was seen to be conspicuously dilated. Even in the areas mentioned above as not being spongy to the naked eye a delicate reticular fibrosis and a spongy structure were seen with a hand lens. The fibrosis was especially great throughout the left upper lobe, which was so shrunken that the lower lobe formed the apex of the left lung. It was also very great in the anterior part of both the upper and middle lobes of the right lung; here it enclosed many bronchi, which were considerably dilated and packed close to one another. In general it was greatest in the anterior and lower portions of the lobes, and there was no appearance of radiation from the hilum. The more fibrotic areas were distinctly more anthracotic than the less, and the shrunken left upper lobe was deeply anthracotic. The areas which were not spongy to the naked eye were of a rusty tinge. Very few small branches of the pulmonary artery could be recognised; most of these were unusually thick but otherwise of normal appearance, a few could be identified as solid cords of pearly-grey fibrous tissue. The larger pulmonary branches projected, and had conspicuously thick walls. When slit open their intima showed numerous opaque yellowish-white flecks and small buttons of atheroma. In the distal portion of the pulmonary stem were a few faint yellow flecks.

The necropsy was performed by Dr. W. W. Woods.

*Microscopic Examination.**

The visceral and parietal *pleuræ* are both greatly thickened by a dense collagenous fibrous tissue, and are intermittently fused. The upper part of the lower lobe of the left *lung* shows no abnormalities except emphysema, and engorgement of the larger capillaries and venules. All the other portions of the lung show a great thickening by dense fibrous tissue of the septa and of the adventitia common to the bronchi or bronchioles and their pulmonary artery. The dense fibrosis extends from the broncho-pulmonary adventitia along the adjacent walls of the alveolar passages and infundibula. Near the bronchi or bronchioles the air cavities have been completely replaced by fibrous tissue or are represented by a few small widely separated cavities. Further out the fibrotic thickening of the walls of the alveolar passages and infundibula diminishes progressively, but it is completely absent in only a very few areas. Such areas appear as islands in the fibrotic tissue. The alveoli with fibrotic walls are lined with a continuous row of oval or cubical cells. Where the fibrosis is greatest and has led to reduction in the size of the alveoli many of the alveoli contain round, desquamated epithelial cells.

The fibrotic tissue in the pleuræ and lung consists of stout collagen fibres and contains few fibrocytes; it shows patchy infiltration with lymphocytes, plasma cells, and a few eosinophil leucocytes.

The bronchioles are dilated. In the anterior part of the upper lobe of the right lung and the lower posterior part of the upper lobe of the left lung they are greatly dilated and are filled with mucus, which contains a variable number of desquamated epithelial cells and an occasional neutrophil leucocyte. Except where the air cavities have been almost completely obliterated by the interstitial fibrosis the respiratory bronchioles, alveolar passages and alveoli are conspicuously dilated; this dilatation is greater in the fibrotic areas than in the islands in which fibrosis is absent.

The number of capillaries is obviously reduced in the fibrotic alveolar walls, and is reduced in proportion to the amount of fibrosis. All capillaries throughout the fibrotic portions of the lung are greatly engorged but the engorgement is most striking in the included islands of lung tissue which are free from fibrosis. Here the walls of the alveoli are greatly widened and are moniliform in outline owing to the great distension of their engorged capillaries. There is much hæmorrhage into alveoli, and there are many small and a few large hæmorrhages into the interstitial tissue. The muscular tissue of the fibrotic portions of the lung is greatly hypertrophied. There is slight anthracosis in the site of lymphatics. Nowhere is there any infiltration with neutrophil leucocytes or any acute bronchitis or pneumonia.

In the *right main bronchus* many of the columnar epithelial cells are distended by mucus, there is a patchy infiltration of the mucosa with lymphocytes, plasma cells, and an occasional neutrophil or eosinophil leucocyte, and the mucous glands are infiltrated with plasma cells and lymphocytes.

* Portions were taken from the posterior border of the lower lobe and from near the anterior border of the upper lobe of the right lung; from the lower part of the posterior border of the upper lobe, including the adjacent part of the lower lobe, and from near the anterior border of the upper lobe of the left lung; from the right main bronchus, including a lymphatic gland; from the pulmonary stem; the right pulmonary artery; the left testicle; the body of the stomach; and the pancreas. After fixation in 4 per cent. saline formaldehyde they were embedded in paraffin; sections were stained with Ehrlich's hæmatoxylin and eosine, Weigert's iron hæmatoxylin, and van Gieson's mixture, Weigert's fuchselin and neutral red and, in some cases, Gram's stain and neutral red. Other portions were put through the Levaditi process for the demonstration of spirochætes, with a piece of congenitally syphilitic liver as control.

Few parabronchial *intrapulmonary pulmonary arteries* happen to be included in the sections. One such artery is occluded by endarteritis fibrosa; the others show considerable musculo-elastic hypertrophy of their intima. Some of the primary branches of these arteries and numerous pulmonary arteries of medium and small size are occluded by endarteritis fibrosa. The occluded lumen in some cases is narrowed, the media being crenated. The occluding tissue is sometimes composed of a reticulum of delicate collagenous fibrils and a few large spindle fibrocytes. It is sometimes sparsely infiltrated with lymphocytes and plasma cells. Usually it consists of very stout collagenous fibres and very few fibrocytes. It usually then contains delicate elastic fibrils. It is almost always canalised, and the canalising vessels usually comprise veins and capillaries as well as an artery. Sometimes, as in the case of the artery accompanying a bronchus, a large artery occupies almost the whole of the lumen of the old artery, being separated from the old media by a narrow zone of fibrous tissue containing capillaries. The canalising veins and arteries have muscular walls. Elastic fibrils are usually present in their walls; the fibrils are delicate and vary in number, but in many arteries they are as abundant as in a typical pulmonary artery. Most of the pulmonary arteries that are free from endarteritis fibrosa, especially the larger, show musculo-elastic hypertrophy of the intima. Secondary degeneration can sometimes be recognised by replacement of some of the muscle fibres by foam cells.

The *bronchial and pleural arteries* are free from endarteritis but usually show intimal hypertrophy. The pleuræ contain many wide veins. If *pulmonary veins* in the septa and pleura have been destroyed by endophlebitis their destruction has been complete, because there is now no recognisable remnant of their walls.

The intima of the *right pulmonary artery* is hypertrophied over four-fifths of the circumference, and is in places twice as thick as the media. Secondary degeneration is indicated by replacement of muscle fibres by many groups of cells which appear to be distended with fat, but paraffin sections are alone available.

The intima of the *pulmonary stem* is hypertrophied throughout the section, and in thickness has a ratio to the media which varies from 1 : 5 to 1 : 1·34. The hypertrophy is formed almost exclusively by the longitudinal musculo-elastic layer of Thoma. Many muscle fibres are replaced by foam cells.

The right *hilar lymphatic gland* is extremely engorged and the sinuses are filled with blood. There are numerous plasma cells in the lymphadenoid tissue.

In the left *testicle* there are large confluent areas of fibrosis. In these areas the tubules are obliterated by a great hyaline thickening of the fibrous layer internal to the elastic membrane, and the obliterated tubules are widely separated by dense fibrous tissue. In the centres of some areas the elastic membrane has been partially or completely destroyed. There is a slight infiltration with lymphocytes, plasma cells, and eosinophil leucocytes, particularly in the periphery of the fibrous areas. The large arteries show intimal hypertrophy; the lumina of many of the smaller arteries and veins are partially occluded by endarteritis fibrosa.

The *body of the stomach* is greatly engorged. In one section there is no other abnormality except an infiltration of the mucosa with plasma cells, which is usually confined to a narrow zone at the surface. In the section including the hæmorrhagic area there is in the submucosa a large area of œdema, dense infiltration with neutrophil leucocytes, and hæmorrhage; the walls of many veins are infiltrated and necrosed. The hæmorrhage and infiltration extend into the circular layer of the muscularis. The mucosa over the area is necrosed and at one spot its deeper layers are packed with neutrophil leucocytes. In the necrosed mucosa there are masses of Gram-positive cocci and bacilli; in the submucosa there are numerous Gram-positive cocci, diplococci, and streptococci in short chains, but only a few bacilli; some of the cocci lie within veins.

The *pancreas* shows a purulent pancreatitis with lipolysis, proteolysis, and hæmorrhage. There is infiltration and necrosis of the walls of some veins. The adipose tissue beneath the peritoneum of the lesser sac is densely infiltrated with neutrophil leucocytes. The duct of Wirsung is surrounded by infiltration and contains concretions and a few neutrophil leucocytes. A few Gram-positive diplococci were found on careful search.

Levaditi preparations.—In the sections so far examined no spironemata have been found; spironemata pallida are abundant in the control sections of syphilitic liver.

Remarks.

The necropsy showed that the essential cause of death was failure of the hypertrophied right heart. That the heart failure had been present for some time was shown by the severe "back-pressure" atrophy of the liver. The purulent streptococcal inflammation of the stomach and pancreas was obviously a subsidiary terminal event. As regards the cause of this terminal infection, the condition of the spleen appears to exclude pyæmia; the most likely explanation is a focal infection of the mucosa of the greatly engorged stomach and an infection of the subjacent pancreas by direct spread; the juxtaposition of the inflammation in the stomach and pancreas brings strong evidence in favour of this view.

The hypertrophy of the right heart, the failure of the heart, and the cyanosis observed during life are adequately explained by the condition in the lungs. First, there was a great loss of alveolar surface. Many alveoli had been completely destroyed by the interstitial fibrosis. Where the fibrosis was less the alveoli were greatly distended. The distension of these alveoli and the bronchiectasis were doubtless due to retraction of the peribronchial and peribronchiolitic fibrotic tissue. Such alveoli as were not fibrotic were distended to a less degree, those which lay as small islands in the fibrotic portions of lung being more distended than those which were not in close relation to fibrosis (the section of the upper part of the lower lobe of the left lung); but the lung in the latter position showed typical vesicular emphysema. Secondly, there was a great loss of capillaries in the walls of the fibrotic alveoli. Finally, most of the pulmonary arteries of medium and small size, and some of the large, parabronchial, were occluded by canalised endarteritis obliterans. These changes could not fail to cause great obstruction to the lesser circulation. Direct evidence of the obstruction caused by the reduction of the capillary area was shown by the intense engorgement of the remaining capillaries and by the intra-alveolar and interstitial hæmorrhages.

The inflammation in the lung had been of long duration. This was shown by the stoutness of the collagen fibres and the paucity of fibrocytes in the fibrotic pleura and pulmonary interstitial tissue, by the presence of elastic fibrils in the inflammatory tissue occluding the arteries, and by the formation of vessels with muscular and elastic coats within this tissue. But the inflammation was still active: patches of infiltration with lymphocytes, plasma cells, and eosinophil leucocytes lie in the pleura and in the interstitial tissue of the lung; the lumen of some pulmonary arteries is occupied by young granulation tissue.

Although no *S. pallida* have yet been found there can be no doubt in view of the histology that the inflammation of the lung, pleura, and pulmonary arteries was, like the inflammation of the testicles, syphilitic. If confirmation were required it can be found in the positive Wassermann reaction, the perforation of the palate, the fibrosis of the tonsils, and the scar on the penis, which at least suggests venereal infection. The syphilitic inflammation of the lung is entirely interstitial; there is no trace in the sections of bronchiolitis obliterans or of intra-alveolar organisation. Further, there is no evidence of its having spread fan-wise from the hilum into the lung.

In most of the pulmonary arteries in the lung that were free from inflammatory endarteritis, in the right primary branch of the pulmonary stem, and in the pulmonary stem itself there was intimal hypertrophy; and the hypertrophied intima was the seat of considerable atheroma. Such intimal hypertrophy and secondary degeneration occur in all cases of obstruction to the flow of blood in the lesser circulation, for instance in mitral stenosis; and they have been in my experience proportional to the estimated degree of obstruction.

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THE RESISTANCE TO MALIGNANT GROWTH.

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In the following paper a brief résumé is given of the results of seven years' work, of which a full account has been already published elsewhere.[1]

The experiments were prompted in the first instance by a doubt whether the cancer cell differs in any essential respect from cells of the normal body. The extreme diversity of cancer, it seemed, is difficult to reconcile with the idea of a specific nature or common causation; and the gradation of its different types from innocent tumours to malignant disease of the most virulent kind points to a perfectly regular descent from one to the other. The histological classification of tumours is notoriously artificial: their propensity when malignant to invade adjacent tissues, to form metastases, or to survive transplantation may be very pronounced and quite distinct as a general rule, but on the other hand is sometimes only feebly developed or even altogether absent; it is scarcely possible to look upon any of these properties singly as absolutely characteristic or fundamental, and the combination of them all is probably rather exceptional. The boundaries between tumour tissue and normal cells are almost as indefinite as those between one tumour and another: three well-known illustrations of this are the dermoid cyst, an evident anomaly of development; the chorion, passing occasionally into chorion-epithelioma; and embryomata, or the tumours which arise from the introduction of embryonic fragments into the tissues of an adult host. The course of evolution rarely leaves behind it so complete a chain of "missing links" between the various products of its operations. Finally, the application of a series of tar products of varying potency may induce hyperplasia, or papilloma, or cancer, or all of these in succession; and the cancer when it develops may or may not prove to be transplantable.

The growth of cancer was for these reasons regarded as of fundamentally the same nature as growth of any other kind, however magnified and distorted and nearly unrecognisable the growth-picture may become. In this connexion the word "growth" is itself ambiguous; for the growth of a tissue must be differentiated from the growth, or condition of multiplication, of its constituent cells. The growth of a cell-population is not merely a question of birth-rate; it is a preponderance of births over deaths. In the normal adult body there is, as a rule, no such preponderance, and therefore no growth; but this is not because there is no cell-multiplication, but because there is an equally high cell-mortality. Even in old age the cells of many tissues continue to multiply rapidly; and the characteristic feature of a tumour is not that its cells multiply, but that their multiplication leads to uncontrolled growth. In the genesis of cancer, therefore, it seemed to be idle to consider only the cancer cell; and necessary first to ascertain the normal method of growth control. For if the transitional stages in tumour malignancy reflect different degrees of failure in the control process, they indicate also that the method of control is seldom if ever completely ineffective. Moreover, if the process of physiological control were understood, it might also be reinforced; and the prevention or even the arrest of malignant disease might in fact be accomplished, not by pharmacological methods in the narrow sense, nor by the methods of bacteriological immunisation, but by the physiological method at work in the normal body for the prevention of excessive growth, of which cancer itself is only an extreme and perverted form.

[1] Heaton, T. B.: Jour. Path. and Bact., 1929, xxxii., 565; See THE LANCET, August 17th, p. 342.

The Control of Normal Growth.

Leaving aside for the moment, therefore, all question of tumours, the conditions first to be reviewed are those which prevail in the normal body.

Tissues which fail to increase, though their cells proliferate, must clearly be subject to some form of restraint, and the process has been described as "tissue tension." It is a description, not an explanation, and implies only that tissues in contact with one another maintain a certain equilibrium, in spite of tendencies to expand which any of them may display. But the manner of this resistance to expansion would not seem to be in doubt, though the blood-cells and blood-forming organs are obviously exceptional, and require control of an exceptional kind. Apart from these, any tissue whose cells are constantly multiplying will expand, like other living colonies, to the limit of the available food-supply, and tissue tension must involve the restriction of this supply. The needs of different tissues in this respect no doubt vary greatly, and include nutrition, oxygen, mechanical support, and the removal of waste products; but so long as these services, comprised under the name of "stroma," are stationary, all tissues dependent thereon must be stationary also. It is therefore striking that most of the tissues whose cells continue to multiply throughout life are epithelia, while the vascular connective tissues are normally static and passive. If growth never occurred the process of tissue tension might be thought to consist simply in this passivity, imposing a limit on epithelial proliferation and differing in various localities only in the pattern of the various supporting and proliferative tissues.

Actually growth is always taking place; almost every organ is capable of hypertrophy and of renewal of activity for the repair of injury. In the skin, for example, the multiplication of epidermal cells is normally limited to the replacement of wear and tear, any increase being prevented by the unyielding character of the underlying stroma; but sometimes true growth occurs, as when hairs are developed at puberty or, as in many animals, with the recurrence of the seasons. In such cases the hair follicles increase in size, in response to the stimulus of a hormone; and this involves growth not only in the specific epithelium, but also in the connective tissue which supports it. The hormone acts directly upon the epithelium, but this in turn induces a reactive increase of stroma. The passivity of stroma, therefore, is only relative; it is overcome whenever the growth tendency of the epithelium receives additional impetus. Similar reactivation of static connective tissue is seen on a large scale in the process of granulation, and in both cases passivity is resumed as soon as the special conditions cease to exist.

An accurate balance, therefore, preserves the passive status of connective tissue stroma, and on this equilibrium tissue tension would seem to depend. The stimulus of epithelial activity tends constantly to upset the equilibrium, but is only in special circum-

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stances sufficient to do so. There must be some agency to counteract it; it cannot be counteracted merely by the inherent inertia of connective tissue. For connective tissue has, in fact, no such inherent inertia at all; when cultured in vitro its cells continue to proliferate indefinitely, and indeed with greater robustness than any other type of cell. The influence which antagonises the stimulant action of epithelia is therefore external; and on the analogy of the numerous growth-promoting factors which are known, both hormones and vitamins, is likely to have a chemical character. It is likely, in fact, to be a hormone or a vitamin itself, the equilibrium of tissue tension being of the common physiological type, between this factor which tends to arrest growth and antagonistic factors tending to promote it; now one predominates, now the other. Furthermore, the growth-promoting influences are multiple, for the epithelia upon which they act are very diverse; but the inhibiting influence which acts upon a single tissue, the stroma, is not unlikely to be single.

A Growth-inhibiting Factor.

Various organs were therefore tested in the hope of obtaining an extract with the property of stabilising connective tissue. The method employed was that of tissue culture, the extracts being added to a nutrient medium in which connective tissue cells (fibroblasts) were implanted; implants of epithelia (from the intestine) were made at the same time as a control, to ensure the general fitness of the medium for cell growth. Nor was the search long or difficult. The extracts were made in 75 per cent. alcohol, evaporated down, taken up in water and sterilised, being freed thereby from proteins and growth-promoting factors which all tissues, of course, contain; and the action in question was shown by all the tissues examined in approximately the same degree, extracts of the liver being perhaps rather more active than those of other organs. In the plain medium, that is to say, fibroblasts and epithelial cells grew equally well; but the addition of extract of any tissue prevented the growth of the fibroblasts without interfering with that of epithelia.

The widespread distribution in tissues of a substance which inhibits growth was not unexpected; but it seemed to point to derivation from the diet rather than to a synthetic origin in the body, and yeast, among other foodstuffs, was tested for its presence. Brewers' yeast was found to contain it, but not bakers' yeast, and a likely source was thus indicated in malt, upon which brewers' yeast is grown. After long use of an extract obtained from yeast, malt was accordingly substituted, and seemed to be preferable, yielding very readily a crude but active extract of fairly constant composition.

Effect on Normal Growth.

An extract being now available with the desired action upon connective tissue cells in vitro, the next step was to apply it in vivo. The suggestion was that this substance inhibits the proliferation of fibroblasts in the body and determines, by its eventual predominance, the cessation of the growth period. If this were so, it seemed that by administration of the extract to young animals the growth-promoting factors might be prematurely counteracted and normal growth cut short. It was administered by addition to the water in the case of aquatic animals, and by intraperitoneal injection to mammals. The effect was noted on the metamorphosis of tadpoles, on the regeneration of amputated parts in newts, on the growth of young rats, guinea-pigs, and rabbits, and on the course of pregnancy in guinea-pigs. The result in every case was the same: with small doses growth was delayed, with larger doses it was completely and immediately arrested; and when the treatment was omitted growth was resumed.

Objection might be made that the effect of injecting a crude extract would be gross poisoning, and arrest of growth from mere interference with appetite and general well-being. Indeed the objection would not be unreasonable, for the doses given were but little less than lethal. It was noticed, however, that the younger the animals the less easily were they affected. The relative dose for a small rat or guinea-pig was three times as large as that required for a half-grown animal; and a curve was obtained in the case of guinea-pigs showing a definite inverse ratio between body-weight and the dose per kilo necessary to arrest growth. So marked a discrepancy, it seemed, would scarcely be consistent with a merely toxic effect; but was only to be expected if the action were specifically upon the growth process, for the energy of growth is at its greatest in young animals. Furthermore, the dose necessary to arrest growth was found to be considerably larger than was sufficient to prevent its resumption, and the dose necessary to arrest the course of pregnancy considerably larger than would be tolerated by non-pregnant animals.

Effect upon Tumours.

The normal function of this factor, it is suggested, consists in preserving the balance of physiological growth, and as such may have some general physiological interest in relation to problems of growth and diet. But its effect when given in excess would seem to be applicable also to the case of growing tumours. For as seasonal or other normal growth is induced by hormones, the growth of tumours is induced by epithelial stimulation in other ways, as by certain irritants; and the effect in either case is to overcome the resistance to expansion of the underlying stroma. If by giving the inhibiting extract in excess this resistance can be raised sufficiently to prevent physiological growth, there would seem to be no reason why the growth of tumours whose demand for stroma is precisely the same should not be resisted in the same way.

Whether the inhibiting extract will be found in fact to have any prophylactic or curative value as applied to human cancer has yet to be determined, and experiments to that end are in progress. Hitherto trial has been made only with transplantable tumours in rats—namely, the Jensen rat sarcoma, and, in a few cases, the rat carcinoma No. 9—and the extract has necessarily been given by intraperitoneal injection. The results were striking enough, tumour growth in several hundred animals being brought very rapidly to a standstill; but the necessary dose was large, since only young rats were used, and after the growth of their tumours had been arrested the animals usually died. The difficulty was thought to be only technical, for in a number of rats which could be induced to take the extract by the mouth complete retrogression of the tumours was obtained. The following facts, moreover, seemed to be of importance: (1) the appearance of the tumours after arrest of growth was one of intense venous congestion, as has been found also after their arrest by radium or the application of heat; (2) whatever the size of the animal the dose necessary to arrest tumour growth was the same as that necessary to arrest its body growth, and in full-grown animals would therefore be comparatively small; (3) an effect on tumours was only obtained with extracts which proved on tissue cultures to exhibit the specific property described, of preventing the growth of fibroblasts.

The Jensen rat sarcoma is no less malignant than the majority of spontaneous tumours; and the experiments therefore suggest that the differences between malignant and normal cells are less important than their fundamental resemblance. A tumour, like any other growing focus, needs a growing vascular environment; it is on this environment that the control of normal growth is exerted, and it is here that resistance may be offered also to the growth of cancer. The inhibiting factor seems to provide a possible agent for making this resistance effective.

Corrigendum.—In Dr. E. Fränkel's article on the Blastogenic Principle in Fowl Sarcoma, THE LANCET, Sept. 14th, p. 539, col. 2, line 50, for "six attempts out of ten" read "out of *twenty-one*."

THE USE OF INSULIN IN THE TREATMENT OF PERNICIOUS ANÆMIA.

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THE importance of liver in the process of blood-regeneration was first pointed out, independently, by Whipple and Robscheit-Robbins, and by Jeney. Whipple and his collaborator were the first to report good results from feeding dogs, made anæmic by repeated bleeding, with fresh liver, while the favourable results of protein-free liver extract were first published in a Hungarian medical journal by Jeney in a communication from the Jobling Institute for Pathology, Columbia University, where he carried out his researches in 1923–24. The paper[1] by Whipple and Robscheit-Robbins was published in May, 1925, and Jeney's work appeared in the spring of the same year.[2] Minot and Murphy in 1926 introduced their successful liver diet, which has since become famous, for pernicious anæmia, but Whipple and his collaborator adopted liver extracts only in 1927. Jeney's researches, performed in 1923–24, partly in collaboration with Prof. Jobling, were therefore the first in connexion with a protein-free liver extract. Accounts of them were published in America in 1927.[3 4] I have emphasised these facts because Jeney's right of priority is in question, and his name is not mentioned in the most important papers and works on the subject. Mouzon[5] alone mentions the experiments of Jeney and Jobling with alcoholic liver extract.

Liver and Insulin.

Of the very numerous proposals for treating pernicious anæmia that represented by Minot and Murphy seems to be the most noteworthy. According to these investigators, liver supplies the materials necessary for building up the cytoplasm of the blood corpuscles and at the same time has a stimulating influence on the bone-marrow, acting in so specific a manner that they consider that any anæmia in which a liver diet is ineffective may be excluded from the class of pernicious anæmia. That liver actually contains substances which promote the formation of red blood corpuscles—in the form of building substances or specific stimulants—is proved by the researches of Jeney and Jobling and by Robscheit-Robbins and Whipple's experiments on animals. Jeney's[6] work shows that the substances promoting blood formation are to be sought in the decomposition products of red blood corpuscles developed in the liver.

It is only natural that the treatment of pernicious anæmia should depend on a series of factors, such as the state at which the patient is received for treatment, his individuality, his reactivity, the regenerative power of the bone-marrow, the duration of the malady and the number of relapses, and this fact must not be disregarded. It explains the relative failures frequently obtained alongside favourable results.

During the past two years we have had a strikingly large number of cases of pernicious anæmia in comparison with former years. Since the essential of treatment must lie in assisting the blood-forming organs and in strengthening the whole body, we thought it advisable to employ a remedy intended to combat the well-known loss of appetite in pernicious anæmia, and for this purpose tried insulin, which we had previously been using in all cases of anorexia. The anorexia and cachexia of our patients made it impossible to begin a liver diet at once, but we hoped to be able to improve their appetite so that they could take it.

In a comparatively short time we had eight patients for treatment. Their treatment and its effects is shown in the Table.

Case 1 was treated with insulin alone (60 units daily) and the number of the red blood corpuscles rose within a month from 770,000 to nearly four millions, the appetite being meanwhile excellent, while the hæmoglobin content also assumed more normal figures. Cases 2, 3, and 4, which were placed on insulin and arsenic treatment, showed results in no way better than Case 1. The rise in the blood count was somewhat gradual, the hæmoglobin values showing rather greater improvement. Case 5 is interesting. During the first 24 days of treatment the patient received 30 units of insulin daily and 1 c.cm. of strychnotonin (a preparation containing arsenic). During this period the red blood cells rose from 850,000 to 1,400,000, and the hæmoglobin percentage from 22 to 28. The patient was then put on a diet including 100 g. of cooked calf's liver daily, with the result shown in the table. Case 6 received 60 units of insulin daily from the first to the 37th day, and 2·5 g. of Richter's perhepar (a liver extract) from the 10th to the 50th day. During the first ten days, with insulin alone, there was no increase in the blood count and hæmoglobin values, though the general condition and appetite were excellent. When liver treatment was started they immediately began to rise, and after a month the patient was discharged in very good health. Case 7 at first responded well to insulin and arsenic treatment, but after a month's progress the red cells and hæmoglobin became stationary. From the 80th day onwards the insulin was stopped and the patient was given 100 g. of Schottmüller's hepatopson daily. It was very striking to note that the number of the red corpuscles increased by 1·5 million during the ensuing 20 days, while the hæmoglobin value declined. In Case 8, owing to the grave condition of the patient, both insulin and liver extract were given from the beginning (insulin 50 units and a spoonful of hepatopson). Both forms of treatment were discontinued within 42 days, but in two months the number of the red corpuscles rose to over five million, although the patient was in a dying state when admitted.

No.	Age in years.	Period of treatment.	Values at the beginning and at the end of treatment.			Daily increase.	
			Hb %	Blood count in millions.	Colour-index.	Hb.	Blood count.
1	36	Feb. 10 to Mar. 17.	15–60	0·77–3·8	1·0 –0·78	1·2	84,400
2	30	Apl. 20 to May 26	28–78	1·14–2·9	1·11–1·21	1·4	48,000
3	55	Feb. 6 to Mar. 17.	35–70	1·4 –3·2	1·13–0·98	0·87	45,000
4	55	Mar. 27 to June 5.	48–70	1·36–2·56	1·55–1·23	0·3	16,901
5	41	July 27 to Oct. 1.	22–65	0·85–4·5	1·23–0·65	0·59	50,695
6	66	Apl. 16 to June 5.	36–82	1·8 –3·9	1·00–1·05	0·92	42,000
7	36	Dec. 1 to Mar. 13.	37–80	1·8 –4·9	0·70–0·80	0·6	41,346
8	36	Jan. 5 to Mar. 21.	21–75	0·73–4·4	1·02–0·76	0·71	45,655

Treatment.—(1) 2100 units insulin; (2) 540 units insulin and strychnotonin; (3) 3060 units insulin, and arsenic; (4) 2200 units insulin, and natrarsen; (5) 690 units insulin, 4600 g. liver; (6) 2220 units insulin, 100 g. perhepar; (7) 4050 units insulin, 2100 g. hepatopson; (8) 1950 units insulin and 3000 g. hepatopson.

The subjective condition improves in a very short time in response to insulin by itself, as well as to the insulin-liver and insulin-arsenic treatments. After taking insulin bulimia sets in, and the vertigo, buzzing in the ears, and general debility disappear; the condition of the patients visibly improves, and the number of red corpuscles and the hæmoglobin content increase (by 30,000–40,000 and 5·10 per cent. respectively per day). The headaches disappear last, but these, together with serious anæmia, are correlated

with the gastro-intestinal disorders, which, as a rule, remain to the end and which are often strongly marked. The constant anorexia can be transformed into bulimia in three or four days by insulin, so that patients want to eat continuously. Return of healthier colour may be looked for on the tenth day; this and the redness of the lips is increasingly pronounced. As the blood count and hæmoglobin values rise there is a fall in the colour-index, and a disappearance of hyperchromatosis, together with a decrease of anisocytosis, megalocytosis, and poikilocytosis, and disappearance of polychromatophilia and normoblastosis. The only symptom which remains to the end, and which it is impossible to influence in any way, is achlorhydria.

I began the insulin treatment with 20–30 units (twice daily), increasing with the improvement in appetite to 40 units, always half an hour before meals. With the use of Richter's insulin there are practically no disagreeable symptoms, such as hyperæmia, œdema, and pains. Large doses, however, entirely destroy the appetite, while there is also the danger of hypoglycæmia. It should be noted that in general the insulin treatment has always an optimal limit. In Case 8 we discontinued the liver diet, mainly because the hepatopson was very trying to the patient, owing to its bulk and unpleasant smell. Later we had recourse to Richter's perhepar, a remedy containing a large quantity of liver substance in quite a small compass (1 g. equivalent to 100 g. of liver), so that the daily dose of 250–300 g. of liver can be administered in the form of a few grammes in wafers without any difficulty. It is now obtainable also in tablet form.

Results of Other Workers.

I thought the publication of these results with insulin would not be without interest, if only because Walinski[7] has hitherto been the sole investigator who has reported satisfactory results from a combined insulin and arsenic treatment with blood transfusion, though Weil[8] has also had a certain degree of success with the same combination. He, however, gave only 5–10 units of insulin. Rathery[9] has reported unfavourable results, and Neuburger,[10] who made unsuccessful experiments in 1924, rejects insulin treatment not merely because the patients are apprehensive of its unpleasant effects, but also because he found that in every case there was pronounced deterioration. According to Imchanitzky, the number of red corpuscles decreases with insulin. Lévai[11] also mentions experiments by Jaksch-Wartenhorst, according to which the use of insulin in pernicious anæmia causes a deterioration in the condition. Varga[12] alone reports the case of a man of 76 in which insulin and arsenic treatment gave good results.

When it is considered that many authorities regard the cause of pernicious anæmia as being a displacement of the blood reaction in the direction of acidosis, which facilitates hæmolysis, and that insulin, on the other hand, increases the alkalinity of the blood (Walinski), the soundness of the insulin treatment appears to be further confirmed.

In a case like No. 8 the use of insulin is of vital importance. On his admission the patient was unconscious, the number of red blood corpuscles being 700,000. Every attempt to feed him failed. After an insulin injection, however, he even took hepatopson, although he fell asleep while being fed. On the third day he began to have a keen appetite, his complexion soon became more healthy, and in a fortnight he was able to leave his bed for a few minutes.

Whilst a liver diet must be regarded as the standard remedy for pernicious anæmia, insulin may be looked on as an indispensable auxiliary.

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(*Continued at foot of next column.*)

Clinical and Laboratory Notes.

LOA LOA INFECTIONS.

A CASE WITH RAPID ONSET OF SYMPTOMS.

By N. A. Dyce Sharp, M.R.C.S. Eng.,
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Attention has often been drawn by Low, Manson-Bahr, and others to the longevity of *L. loa*, and to the lengthy period which may elapse before either symptoms or infection of the blood by filarial embryos becomes manifest. This period may amount to four or more years, and worms have been removed from beneath the conjunctiva of persons who have been outside an infective area for 12 and even 15 years.

On the other hand, little attention has been paid to the minimum period which must necessarily elapse between the bite of the infected chrysops and the moment when the first symptoms appear. The principal symptom, apart from pain and discomfort in the eye when a mature worm happens to pass across it beneath the conjunctiva, are certain rather odd enlargements known as Calabar swellings which most commonly affect the forearms and wrists but also occur in the legs, trunk, and face, and even under the scalp. In an endemic area their appearance is so characteristic as to make the diagnosis comparatively simple in almost every case. Often they arise in a night, giving a bloated, œdematous appearance to the affected part. While objectively they exhibit many of the signs of an acute inflammatory condition, the subjective sensations are relatively trivial, and in a large proportion of cases there is no actual pain or tenderness, but merely stiffness with a feeling of weakness. They never lead to suppuration, and as a rule they disappear as mysteriously as they arise in 50 to 70 hours.

We are at present very far from knowing their true pathology. Manson, who described the worm in 1891, believed that they might be caused by the emission of myriads of larvæ by the pregnant female lying in the connective tissue. Others have suggested as a cause the death of the mature worm and the setting free of unknown toxins. It is proposed to show that in the light of the case given below both these theories are untenable.

Filaria loa is manifestly long-lived and, according to Manson-Bahr, development of the larva in the human body is so slow that full maturity is not reached for several years. In support of this statement he points to the well-established fact that the offspring of the worm may not appear in the blood as microfilariæ for seven years, while the adult parasite itself may not appear for four or more years. Further, infected children rarely show embryos in the blood though immature worms may be found in the tissues. These facts would lead one to expect a period of several years at least to elapse between the date of infection and the appearance of Calabar swellings if the latter are caused by mature or parturient filariæ.

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3. Jeney and Jobling, J. W.: Proc. Soc. Exper. Biol. and Med., 1927, xxiv., 733; Jour. Exper. Med., 1927, xlvi., 839.
4. Jeney: Jour. Exper. Med., 1927, xlvi., 689.
5. Mouzon, J.: Presse Médicale, 1927, xxxv., 1554.
6. Jeney: Zeit. f. d. ges. exper. Med., 1928, lx., 102.
7. Walinski, F.: Deut. Med. Woch., 1926, lii., 1462.
8. Weil, E.: Bull. et Mém. de la Soc. des Hôp. de Paris, 1927, xliii., 1169.
9. Rathery, M.: Ibid., 1122.
10. Neuburger, J.: Deut. med. Woch., 1927, liii., 2078.
11. Lévai, M.: Gyógyászat, 1927, lxvii., 308.
12. Varga, J.: Ibid., 1928, lxviii., 247.

The following case is cited to show that the classical symptoms of loasis may appear long before the larvæ can have reached maturity, and certainly before reproduction could have occurred. The case is interesting, not because it is uncommon, but because the dates are so unusually definite (thanks to the patient's diary), and the symptoms have been observed at intervals by the writer for over nine months.

A. B., aged 23, paid his first visit to the tropics in 1928, landing at Port Harcourt on May 2nd. He arrived at Ikom on May 18th, which was the first place in which he might have encountered a chrysops. But though already well aware of the little red fly, he has no recollection of having been bitten by it until the first week in June. The earliest possible date of infection, therefore, is May 18th, but the most probable date is July 10th, when he was severely attacked by chrysops at a village in the dense bush.

On July 17th—that is, one week after the most probable infective date and 61 days after the earliest conceivable date of infection—he noticed his right knee was stiff and swollen, and on this subsiding the left arm showed a swelling in the middle of the forearm. As soon as that had disappeared a swelling of the same kind appeared in the left leg. Such swellings have appeared at short intervals ever since and never has the interval extended to a month.

On August 31st he had to wear his arm in a sling owing to the pain in the swollen forearm, which subsided painlessly next day. A few days previously the fingers, wrists, and thigh had been affected.

In April, 1929, the right wrist was swollen, and for the first time there was a sensation of something moving near the knuckle of the ring finger which was swollen and stiff, and the patient said it felt as though the skin over it would burst. Though usually the swellings had been painless, this one was definitely painful, and owing to the swelling the ring finger could not be flexed, and while writing was difficult, golf was impossible. A note made at the end of April recalls the fact that this was the 19th day of a swelling which, starting in the left wrist, crossed quite abruptly to the right about six days before, whence it spread to the ring finger. There was, as usual, no œdema, but the swelling was hot and quite definitely painful.

On May 25th the patient complained that a swelling beneath the scalp had given him a headache. This swelling appeared over the right parietal bone on the 23rd, disappeared on the 24th, and reappeared over the left parietal on the 25th. At a final examination on June 5th the left ring finger was still slightly stiff. No worm had appeared under the skin or conjunctiva, and apart from an eosinophilia the blood picture was normal.

We are still very far from a solution of this curious phenomenon.

ENLARGEMENT OF THE LEFT AURICLE OF THE HEART.

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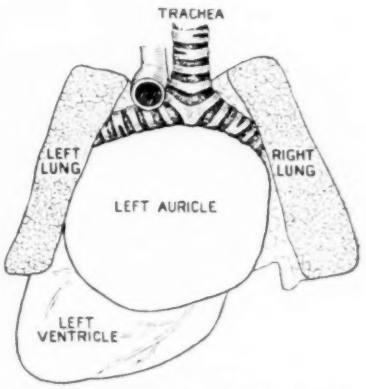
AND
T. S. KEITH, M.B. LOND.,
PATHOLOGIST TO ST. MARY ABBOTS HOSPITAL, KENSINGTON.

ENLARGEMENT of the left auricle of the heart was recognised and described by early medical writers. The association of left auricular enlargement with mitral stenosis was appreciated in the writings of Corvisart and Laënnec, and nowadays the radioscopic demonstration of left auricular enlargement is considered an important sign in the recognition of mitral stenosis. Various complications may arise from distortion of the upper mediastinum as the result of enlargement of the left auricle. Compression and displacement of the œsophagus, paralysis of the left recurrent laryngeal nerve, and compression of the left bronchus have been described by various authors. The case which we report is one in which the left main bronchus was compressed by the enlarged left auricle, and collapse of the left lung resulted. Bronchial compression by an enlarged left auricle has been known for nearly a century. The first report "on the morbid flattening or compression of the left bronchus produced by dilatation of the left auricle" is by J. W. King in the *Guy's Hospital Reports* of 1838. Four cases were described; three of them at autopsy showed definite evidence of mitral stenosis and the fourth was thought to be a case of congenital heart disease. In 1867 Friedereich reported the case of a girl with marked mitral stenosis in which the clinical diagnosis of compression of the left main bronchus had been made in 1850, and confirmed at autopsy four years later. Taylor, Sansom, and many other writers refer to the condition in association with mitral stenosis. Stoerk,[1] in 1910, in a study of the anatomical relations of the mediastinal contents, demonstrated that the left auricle made up the posterior and superior parts of the heart, and that the main bronchi were in close relation just above it and that the left main bronchus normally rested on the upper surface for a short distance (see Fig. 1). In 1901 Owen and Fenton first described extreme enlargement of the left auricle to the right. Shaw, Bramwell, East, and Lutenbacher have described further cases, and recently Bedford[2] has described two cases in great detail and given a complete review of the literature. Last year Murray Steele[3] reviewed the literature and gave a clinical description of a case suggesting bronchial pressure due to an enlarged left auricle.

FIG. 1.



Dorsal view of the heart showing widening of the bifurcation of the trachea by large left auricle. (After Stoerk.)

Résumé of Case Notes.

The patient was admitted to St. Mary Abbots on April 27th, 1929, as a case of active rheumatic carditis. For three or four months she had had vague transient pains in the arms and legs, and a cough but no sputum. She was losing weight. For two months she had kept in bed at home with persistent tachycardia. She was a pale, "toxic," wasted child, with a temperature of 99° F. There was no gross congestive failure. Exercise tolerance was very poor, the heart was enlarged, the apex beat heaving, mobile, and outside the nipple line in the left sixth space; the pulse-rate was 100 per minute. The heart beat was regular with frequent extrasystoles, a diastolic thrill at the apex, full diastolic bruit, accentuated first sound, systolic bruit and modified second sound. At the base the pulmonary second sound was slightly accentuated but no bruits were heard. The lungs were clear, and the liver and spleen were not palpable. On May 7th the apical rate was 160 and regular, and showed no alteration with change of posture or after moderate exercise. The lungs were clear. On May 9th there was slight pyrexia and frequent extrasystoles, but the tachycardiac condition remained unchanged until May 29th, when a definite area of bronchial breathing was found in the left scapular region, the extreme base being clear. There were no added sounds, but whispering pectoriloquy was heard over this area. Movement of the left chest was fair. The temperature showed an occasional spike of 100°.

Radiography (Fig. 1) showed a large heart of "mitral-stenotic" shape and lungs clear except for doubtful increased density in the middle of the left lung area.

A tentative diagnosis was made of collapse of the left lower lobe, or possibly broncho-pneumonia.

On June 5th the area of bronchial breathing in the left lung had markedly increased, extending practically to the disease of the lung. The circumference of the left chest was less than that of the right and movement was impaired. There was very little yellow sputum. The temperature went up to 100°. The heart-rate was 120, regular. No pupil

[1] Stoerk, O.: Zeit. f. Klin. Med., 1910, lxix., 32.
[2] Bedford, D. E.: American Heart Journal, 1927, iii., 127.
[3] Steele, J. Murray: Ibid., 1928, iv., 53.

changes and no difficulty in swallowing were noted. On aspiration of the left chest 5 c.cm. of clear fluid were obtained. This contained a large amount of albumin, erythrocytes, and occasional polymorphonuclear and some mononuclear cells, but no tubercle bacilli. Cultures were sterile, as was also the blood culture. The sputum contained no tubercle bacilli or streptococci and little pus. A blood count showed 5,744,000 red cells and 6148 white cells made up of: polymorphonuclear cells 70 per cent., lymphocytes 22 per cent., and large mononuclears 8 per cent. The colour-index was 0·7 and the hæmoglobin 80 per cent.

A diagnosis of collapse of the lower lobe of the left lung was made.

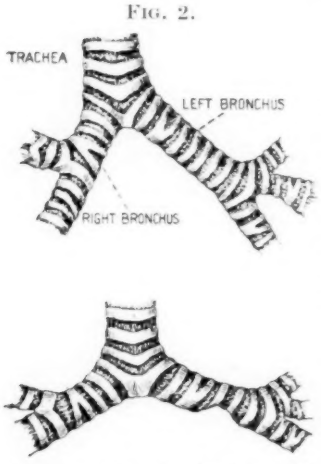
On June 18th the signs were as before and included a few coarse crepitations at the base of the left lung. Later signs of gross congestive failure appeared. Digitalis and leeches were ordered, but on July 9th the patient died.

Autopsy by Dr. KEITH.

The general development was normal for the age. There were a few recent pleural adhesions on both sides, and some small patches of partly organised lymph. The right lung was intensely œdematous and congested, and showed a recent infarct at the apex of the right lower lobe, covered by a patch of pleurisy. The changes in the lung were recent and did not suggest a broncho-pneumonia. The lower lobe of the left lung was collapsed; not to that extreme degree seen in pneumothorax, but it was completely airless and no fluid could be expressed from it. The upper lobe was very slightly congested. The aorta and œsophagus appeared normal and healthy. The trachea contained much mucus but was otherwise healthy. On opening the posterior surface of the left bronchus a large blood-clot was found. This proved to be the contents of the left auricle, which was very greatly enlarged and had come into relation with the posterior surface of the left bronchus. Further examination of the left bronchus showed that there was—at about ¼ inch beyond the original bifurcation of the bronchus—a definite kinking, the kink being at the point where the left auricle had been pierced while opening the bronchus. There was evidence of a considerable degree of obstruction at that point, although the removal of the organs from the body had partly reduced it. The right bronchus was normal.

The heart was greatly enlarged and weighed 15 oz. In situ there was marked enlargement to the left, fullness in the pulmonary area, and slight enlargement to the right. The pericardium contained half a teacupful of fluid. There was a patch of pericarditis over the apex, which was united to a corresponding patch on the parietal pericardium by a thin fibre ¾ inch long. The right auricle was slightly enlarged. The left auricle was very markedly enlarged upwards and to the left, and contained a large clot of blood. The exact size could not be made out. The right ventricle was slightly enlarged. The left ventricle was markedly enlarged and its walls much thickened. No gross valvular disease was present. The mitral valve was widened. In the fresh specimen three fingers and in the hardened specimen two fingers could be passed through the mitral orifice with ease. The mitral valve was thicker than normal and showed some roughening at its edge. The chordæ tendinii were definitely shortened and thickened. The aortic, tricuspid, and pulmonary valves appeared competent and normal in structure. There was some free fluid in the abdomen, and the liver and spleen showed evidence of congestive failure.

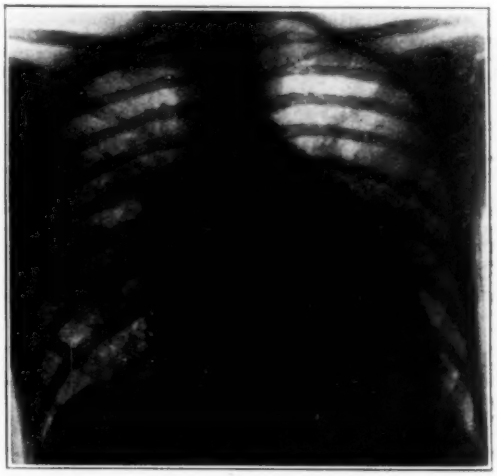
FIG. 2.



Anterior view of trachea and bronchi. Above: normal condition. Below: widening of interbronchial angle.

The clinical picture was one of active rheumatic carditis. The clinical signs of persistent tachycardia, frequent extrasystoles, and at one time a continued ventricular rate of 160 per minute, unaffected by exercise or change of posture and possibly constituting evidence of auricular flutter, suggested particular involvement of the auricular musculature in the disease process. The physical signs were those typical of mitral stenosis, especially the localised apex-beat, the diastolic thrill, and the full diastolic and systolic bruits. The terminal signs denoted left ventricular failure. The radioscopic appearance in the antero-posterior view was that of mitral stenosis. Unfortunately with the technical facilities at our disposal an oblique view could not be taken.

FIG. 3.



Radiogram showing enlargement of the left auricle.

At autopsy the picture was that of rheumatic carditis; a large heart with a wide but thickened mitral orifice, showing no evidence of mitral stenosis, and a very large left auricle. This is an association which I have never seen and to which there is no reference in the literature. A large left auricle is invariably described in association with mitral stenosis, and is exemplified by the cases described by various clinicians. The radiological appearance of "mitral stenosis" was shown although at autopsy stenosis of the mitral valve was not present. Collapse of the lower lobe of the left lung due to constriction of the bronchus by the pressure of a large left auricle—as in this case—is rare.

Our thanks are due to Dr. Remington Hobbs for permission to publish this case.

THE MENTAL FACTOR IN BRONCHIAL ASTHMA.

REPORT ON TWO CASES.

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THE following notes demonstrate the important part which a mental factor may play in the causation of bronchial asthma:—

CASE 1.—The patient was a married youth, aged 27. When seen in November, 1926, he had been suffering from almost daily attacks of the disease for 18 months and his condition had been diagnosed as bronchial asthma by three of the leading physicians in Cairo. The disease started with daily attacks of panting which used to come on in the morning half an hour after leaving bed; they lasted about two hours each and were accompanied by profuse sweating, running from nose, and coughing with bringing up of phlegm. The attacks increased in severity and two months later the patient began to wake up suddenly about 2 A.M. with a feeling of suffocation, dyspnœa, wheezing in the chest, cough, expectoration, sweating, and coryza. After treatment by different doctors for a year the attacks became

less severe and gradually shifted their time of onset until they were occurring regularly every morning about an hour after leaving bed.

By superficial mental analysis I was surprised to find that the patient, who is known to be outwardly calm, is a neurotic person who has been subject to vague fears since childhood. He readily admitted this after first agreeing to the suggestion that the mild attacks of his illness resembled very much the state of a frightened or anxious person. These fears had their origin in infancy when he was often threatened with devils and other weird beings by an ignorant nurse. He used to be particularly afraid of staying or walking in the dark, and therefore was in the habit of having a light in his room all night. About the age of 14 or 15 those fears seemed to have centred about his father, who was an unreasonably severe parent.

The boy would wake up with the impression that a person dressed in a red gown or cloak, like the one used by his father, was standing by, or advancing towards, his bed, and he used to feel very frightened, covering up his face and holding his breath until the apparition moved away. Up till the time I saw him the patient could not put out the light while alone in his room and he became panicky if he heard the slightest sound outside during the night.

Further questioning brought out what I consider the real explanation for the onset of the attacks of asthma 18 months before. This was an incident, about a fortnight before the onset of the illness, in which the emotion of fear was prominent. It appears that his wife was one evening passing a room in their flat where soiled linen was kept, and having become the victim of an illusion that a turbaned stranger was in that room, she screamed and shouted for help. The patient came along and though he armed himself with a broomstick and tried his best to overcome his timidity, he could not bring himself to enter the room. At last neighbours—chiefly women—came on the scene and entered the room to find that the turbaned person was nothing more than soiled clothes thrown carelessly on the edge of a basket.

During further interviews I ascertained that the young man was experiencing dreams causing him to fear for the life of his child or for his own safety, and that he often woke up in a state of terror; after leaving bed in the morning he found himself in a state of anxious expectation which was relieved by an attack of asthma. He also noticed that his fear and anxieties were much less after his illness started. These observations are interesting as they tend to confirm those of Millais Culpin. Another fact brought out during analysis supports W. McDougall's statement that fear alone probably does not produce phobia; the incident causing it must be such as to evoke self-reproach, shame, or a sense of guilt. In the present case fear was admittedly accompanied by a sense of shame occasioned by the patient showing cowardice before his wife and women neighbours.

Treatment followed the lines of explanation, persuasion, and re-education, and in three weeks the patient gave up all medicines and was leaving home every morning for his work without waiting—as he used to—for the attacks to show themselves. For over a year his condition has been almost normal.

CASE 2.—In January, 1928, I saw a nurse, aged 17, working at a mental hospital, who gave nine years' history of typical attacks of bronchial asthma which came on once every week or fortnight, each lasting from one to four days. By superficial analysis I was surprised to find that about three months before the onset of her illness she was on an errand to her people's neighbours one afternoon when a big dog attacked her in a closed hall with no way of escape, and bit her in the leg. She was in a state of terror and fell down unconscious, and when she recovered ten minutes later she felt a sense of suffocation. She then stayed in bed for three months with disturbed sleep and a frequent sensation of fear whenever anyone entered her room at night; at the same time she used to have fearful dreams, waking up in a state of terror and with a feeling of suffocation. After leaving bed and getting about she began to get typical attacks of asthma.

In a later interview the patient said that the attacks often came on a few hours after being approached and threatened by a certain inmate of the hospital, who was particularly big and violent—a situation resembling that of the previous accident. She also said that before joining the service she used to get the attacks after any sort of unpleasant surprise—e.g., after becoming unexpectedly aware of another person standing behind or following her, or after anyone suddenly entered her room while she was ill in bed. She had never related her fear-evoking experiences to anyone, because she always thought it a great shame to feel afraid. I ascertained that she was delicate in health long before the accident and that as a child she was subject to vague fears, especially of darkness. She ascribes these to the way she was brought up during childhood, when the belief in mythical and weird beings was constantly ingrained in her impressionable mind.

These and similar points in the patient's history gave me the clue to the lines on which to treat her psychologically, and by persuasion and explanation many of her faulty ideas and beliefs were corrected. She has now been free from attacks for a year.

These two cases represent almost my whole experience of bronchial asthma, which makes the points of similarity between them seem the more curious. Both patients are of neurotic constitution and gave histories of attacks of fear or anxiety; and there is little doubt that if the analysis were carried further with them more material would be forthcoming to explain much that is abnormal in their disposition. Both developed their asthma after incidents in which fear showed itself prominently and evoked—through the accompanying feeling of shame—an acute internal conflict which was solved by the onset of a bodily illness, this largely substituting itself for the attacks of anxiety. Why they should develop asthma rather than another illness is a pertinent question which leaves open the possibility of a pre-existing physical tendency. Both have undergone some sort of psychotherapy which resulted in more or less complete relief.

The general practitioner is much more liable to meet with cases of bronchial asthma than the psychotherapist and I am writing these notes with the hope of interesting him in an aspect of the disease, which may often be the deciding factor in its caustion or in the precipitation of its attacks.

Medical Societies.

MEDICAL OFFICERS OF SCHOOLS ASSOCIATION.

A MEETING of this Association took place in the rooms of the Medical Society of London, Chandos-street, on Oct. 4th. In the absence of the President, Dr. L. R. LEMPRIERE took the chair.

Mr. SYDNEY SCOTT opened a discussion on the

SCHOOL-BOY'S EAR IN CLINICAL PRACTICE.

He projected on to the screen a number of diagrams showing the auro-nasal regions and their relations, and photographs of pathological conditions of those parts. The most important aspect of the subject was the early recognition of acute infections of the ear. Most people now recognised the advisability of incising the drum membrane in acute inflammations. Probably it had often escaped incision in the past because it was not inspected with a sufficiently strong light. Now that excellent means of examination were available, the drum should be systematically examined by the practitioner in all cases of ear trouble. Students should carry specula and mirrors for this purpose, and should not consider the examination of a patient complete until these had been used. The need of such a routine examination was especially great in fever hospitals. Many children with otitis media did not complain of pain, and were not sufficiently deaf to call attention to the ears, though the membrane was found to be bulging. Others, of course, were noticeably deaf.

Mr. Scott described the case of a boy who complained of slight pain in his ear; a little oil was put into it, and no further treatment was given. The temperature rose and was accompanied by a good deal of head pain; the school doctor thought he must have meningitis, and asked a neurologist to see him. For a week his temperature was between 103° and 104° F. Absence of opisthotonos and reflex signs excluded meningitis, and the neurologist had the patient's ears examined. One drum was bright red and

bulging, though the boy said he had no pain in the ear. On puncturing the drum pus spurted 10 inches, and only after its release was pain felt. Evidently the pent-up pus had caused anæsthesia and the absence of local pain gave a false sense of security. A mastoid operation and other treatment became necessary, since the patient had septicæmia and an infected cerebro-spinal fluid, but eventually he recovered.

In Mr. Scott's student days attendance at the ear department was not compulsory, and the general impression was that all the needed instruction could be obtained from a book—a very fallacious idea. One practitioner had estimated that 25 per cent. of his cases required some experience in ear work. There existed a curious optimism with regard to ear cases among practitioners. A shrewd observer had assured him that practically all his ear cases got well without trouble; there was earache, then discharge, and finally recovery. Ear surgeons, however—probably because the severe cases came to them—took a more pessimistic view. Mr. Scott gave the following example of the kind of case not infrequently seen by the otologist:—

The patient, a boy who had just left school, had been bathing and said that some water had entered his ear, which was not inspected. He went to the theatre that evening and in the night he awoke with intense ear pain. On the following evening the ear began to discharge, but the temperature was more or less normal. On the next evening he felt tired, and two days later he was comatose, and died in that condition without any active steps having been taken. Mr. Scott had been called in, but much too late, since death occurred before the boy could be put on to the operating table. At the post-mortem examination the whole tympanic cavity and all the air cells were found to be full of pus, which, even after death, was under considerable pressure, and the whole cerebro-spinal system, from the frontal lobe to the cauda equina, was œdematous. The presence of streptococci was demonstrated.

Cases of acute otitis media thus called urgently for recognition and attention in the early stages; they should be drained at once without waiting for com plications; they should, in fact, be dealt with on the same principles as any other accumulation of septic material. It was a great mistake to wait for the pus to burst through; it might not do so, but might take a more dangerous course. Conservative treatment was not nowadays justifiable. It could not be too clearly emphasised that incision of the drum did not itself cause deafness, and parents' objection to incision on this score could safely be set at rest. The idea arose from the fact that in the past incisions were not made until disease had produced changes in the ligaments of the ossicles or destruction of the round window. In some cases the drum membrane did not bulge, but with a good light the observer could sometimes see pus on the other side of the drum; in these cases the prognosis after the fluid had been released was very good. If delay in evacuating fluid had occurred it was desirable to open the mastoid.

Discussion.

The CHAIRMAN referred to the need of a campaign against unclean noses, since congested and dirty conditions of the nose were the origin of many cases of ear trouble. In his experience of public school-boys otitis media could undoubtedly exist without any complaint having drawn attention to the ears. In 36 per cent. of his cases of acute otitis media the first ear complaint was of otorrhœa, especially at night time, pus being seen on the bed linen in the morning. Inspection of the ear should be carried out, not once but from day to day. Eight per cent. of the cases eventually needed a mastoid operation. Ear cases were among the most serious which occurred in schools, and the question arose whether paracentesis ought to be done on every patient who complained of earache. Clearly it was needed for the virulently red and bulging drum, but a large number of cases had an abscess of the ear which resolved without interference. Fully 60 per cent. of his cases were of that kind. In young people of school age the meatus might be very narrow or abnormally curved; hence a proper examination was difficult or impossible, and one could not be sure whether the lesion was due to boils close to the drum or to some other trouble such as an accumulation of wax. He would like to know just when a mastoid operation was indicated. In his practice, if otorrhœa persisted more than three days and the temperature remained raised, he called in a surgeon, but it was not feasible to call in an otologist to every doubtful case. What was the significance of a sagging postero-superior wall? He asked for opinions on the value of otalgin; he regarded it as dangerous because it constricted the vessels.

Dr. G. E. FRIEND said he would like to hear more clearly defined the kind of cases which it was safe to leave without performing paracentesis. During 11 years he had done the operation on every case of ear trouble except where the drum looked normal. The average time of healing after the puncture was three to four days, the only other treatment being swabbing out with spirit and boric drops. Of 344 cases, only three had required a radical mastoid operation. He would like to know what was the best treatment for a chronically discharging ear, in the absence of a raised temperature or localising signs. He had had good results from insufflations of bismuth subnitrate.

Dr. J. LAMBERT asked whether a general anæsthetic was always necessary for paracentesis, or whether a local anæsthetic sufficed. He agreed as to the unclean condition of the noses of most of the school population, and thought preventive measures should be directed chiefly to the nose, and especially to the correct way of blowing the nose. Boys who had had ear or sinus trouble should be warned not to dive or swim under water.

Dr. F. G. HOBSON asked about the value of regular morning gargles or snuffles. He had thought this a valuable procedure, but Dr. J. A. Glover did not recommend it.

Dr. A. I. SIMEY said there must be many cases of ear trouble which got well without paracentesis, and spoke of the value of applying ice-bags in cases of acute inflammation of the ear.

Dr. GRAHAM FORBES asked whether the leech behind the ear was at all extensively used now in these cases. He would be glad to hear Mr. Scott's experience on the frequency of ear trouble following visits to a swimming bath. A surgeon in Freiburg traced a number of cases to swimming baths, particularly to those containing unclean water. Dr. Hastie had carried out experimental work on guinea-pigs, injecting the middle ear of the animal with water from a swimming bath, and had in that way produced acute otitis. No doubt the lowered resistance induced by the cold water favoured the onset of the inflammation.

Dr. G. L. BUNTING asked the significance of a continued high temperature after paracentesis; also whether the persistent pulsation afterwards had any serious import.

Dr. W. ATLEE said that a particular kind of ear seen in epidemics was that in which the boy complained of earache for an hour or two, and showed a very dark bleb on the drum. Shortly after the drum ruptured and the boy became comfortable. He wanted to know whether these drums should be incised. He added that for many years the Thames had not been so dirty and empty as this year, nor had so many people bathed in it; yet there had been fewer "acute ears" this summer than for a number of years past. He thought that medical practitioners should carry auroscopes.

Reply.

Mr. SCOTT, in reply, said he never incised a drum unless he saw some adequate reason, some change which was not present in the normal membrane. In some acute cases one was quite justified in waiting before incising. When inflammation of the middle ear was present, the exudation drained much better down the Eustachian tube in some cases than in others. Anatomical differences and varieties of bones added to the difficulties. He had incised a drum

within seven hours of the onset of otitis, but that did not prevent his having to operate later for severe mastoid disease. In some cases it was not safe to wait a week after incising the drum before operating on the mastoid. It was a good working rule to hold one's hand for about five days; whether the mastoid operation should be done earlier depended on whether the patient was very toxic. A good rule was that if the deep part of the meatus sagged the mastoid must be opened. He did not intend to deal with the chronic ear on this occasion. The cessation of an ear discharge was sometimes due to the bursting of a bulla. He did not pin his faith to any particular material for swabbing and syringing the ear. In cases which were painful syringing should be deferred for a few days. For incising the drum he now always used a general anæsthetic. He did not think the wrong method of blowing the nose caused otitis media; if the drums were intact when the nose was blown, infective material could not be injected along the Eustachian tube and into the ear. The routine use of gargles and snuffles was a matter which did not come into his experience; medical officers of schools were themselves in a position to supply valuable information on those points. He had ordered leeches only once in 25 years; he did not favour their use.

ROYAL SOCIETY OF MEDICINE.

SECTION OF THERAPEUTICS.

A MEETING of this Section was held on Oct. 8th, when Dr. P. HAMILL delivered a presidential address entitled

SOME PRINCIPLES OF THERAPEUTICS.

He pointed out that an accurate appreciation of the underlying conditions is essential as a basis for rational treatment. Departures from the normal physiology may be but manifestations of compensatory processes and attempts at "correction" are not then helpful but may hinder recovery. A high blood pressure may be necessary in a given case; nitrites will then be harmful. Antipyretics are little used in fever nowadays; on the contrary fever, artificially induced, may even be beneficial, for example in the treatment of general paralysis by malaria, and in those conditions which are improved by protein shock therapy. Many conditions which call for treatment are the result of previous illness. Damaged organs must be sustained and protected from further injury, and here lies the importance of eradicating septic foci—e.g., the removal of infected tonsils in rheumatic heart disease. Where part of a gland of internal secretion has been destroyed, the effects of the loss may sometimes be circumvented if its active substance can be isolated and easily administered; thyroid gland or thyroxin given for myxœdema, and insulin for diabetes, are good examples. Disorders of infective origin well illustrate therapeutic principles, for elimination of the cause lies for the most part within the sphere of preventive medicine. In the therapeutic sphere direct attack on organisms within the body has been made with success in many protozoal infections—e.g., malaria and amœbic dysentery. Organic arsenic preparations have proved valuable in syphilis and relapsing fever, and antimony compounds in leishmaniasis. In bacterial infections direct attack has been less fruitful; urinary antiseptics and mercurochrome are but partial successes, but the results obtained with sanocrysin in tuberculosis and chaulmoogra in leprosy augur well for the future of chemotherapy. To confer or exalt immunity is perhaps the ideal method of coping with infection if the cause cannot be eliminated or directly combated. Prophylactic immunisation and serum therapy have been very successful in many infections, but fail to fulfil all demands, owing to their inherent specificity, and in some cases owing to the brief duration of the immunity conferred. We have as yet no Mithridatium. For many infections immunising agents of sufficient potency have not yet been developed, and the body must, therefore, rely on its own powers of resistance.

To raise resistance to a high pitch and maintain it there should be our constant aim. Can it be said that adequate attention is devoted to the problems involved? Nutrition, elimination, rest, and general hygiene are the foundations on which resistance to infection and the power of developing immunity are based. Observations by Edward Mellanby and his colleagues indicate that deficiency of vitamin A in the dietary lowers resistance to infection in experimental animals, and a generous supply of this vitamin to patients with puerperal septicæmia is said to have lowered the mortality to zero in a series of cases. In a London business house during the influenza epidemic of the early part of this year a preparation rich in vitamins was supplied to those who desired to take it. There was hardly an absentee owing to influenza or "cold" amongst those who availed themselves of the offer. The conclusion that diet is a large factor in controlling resistance to infection and the development of immunity may fairly be drawn, and the complete proof of this proposition will be a therapeutic advance of the first magnitude. The consumption of milk, dairy products, and oily fish in this country is far too small; incidentally, advocacy by the medical profession of dietary improvement will benefit agriculture as well as the health of the community. Rest is still underrated as a factor in treatment. The widespread use of hypnotics is disquieting; the avoidance of the necessity for their use is desirable. In spite of the importance of quiet, especially for the sick, hospitals and nursing homes still mention the fact that "trams pass the door" as a recommendation rather than a drawback. The rebuilding of hospitals in the inner zones of large towns is surely not consistent with the requirements of rest and hygienic surroundings. The removal of wards to the outskirts of the towns, and the erection of less permanent buildings which can be rebuilt and modernised every 40 or 50 years according to the advance of knowledge and changing conditions is surely a way of progress that demands consideration.

BRITISH MEDICAL ASSOCIATION.

ANNUAL MEETING IN MANCHESTER.

(*Continued from p. 713.*)

SECTION OF TUBERCULOSIS.

Apical and Subapical Tuberculosis.

Dr. D. P. SUTHERLAND (Manchester) presiding, Dr. MAURICE FISHBERG (New York) opened the discussion. Pathological anatomists and clinicians had, he said, long known that the number of people with tuberculous lesions in the lungs was much higher than recorded. The vast majority of tuberculous lesions were found in the apex of the lung and remained in that region. Nearly all cicatrised lesions which remained inactive and gave no trouble during life were in the apex. These lesions were often found clinically, and with the aid of X rays during periodical examinations of healthy persons, which were becoming the vogue in the United States. In patients with non-pulmonary tuberculous lesions, sent for chest examination, changes in resonance were almost invariably found at the apex of the lung, along with altered breath sounds and, perhaps, small adventitious signs; but such patients hardly ever offered significant pulmonary symptoms. In these cases, if death ensued because of the tuberculous infection, it was the result of acute pneumonic phthisis or more commonly miliary tuberculosis. Similar apical lesions were found among persons who suffered from frequent "colds"; they might spit blood and

have tubercle bacilli in the sputum, but with or without therapeutic intervention they did well. It was such cases as these which were diagnosed as tuberculous by the ultra-cautious physicians, and supplied the material for any "cure" which happened to be introduced at the time. They also supplied the "early" and the "curable" cases considered suitable for sanatorium treatment. They were apparently the residua of childhood infection which had become obsolete. While 10 per cent. of civilised mankind died from active and progressive tuberculosis, it had been shown that only about 7 per cent. of the persons with apical lesions developed active tuberculosis or died from the disease.

Turning to subapical lesions, Dr. Fishberg remarked that valuable time might be lost in the diagnosis unless microscopic examinations of the sputum revealed tubercle bacilli, or unless X rays disclosed a soft clouded patch isolated in the midst of apparently healthy lung tissue just below the clavicle, often towards the axillary portion of the lung. The nature of the patch was broncho-pneumonic, of the type seen in primary tuberculosis in children or in tuberculous pneumonia in adults. Over 60 per cent. of subapical lesions manifested themselves in persons under 25 years, as against 36 per cent. of apical lesions. Over 35 years the percentages were 11 and 32 respectively. Under 25, unless a good radiogram was taken, or the sputum found positive, the case was missed. He stressed the importance of X ray examinations; in the United States every tuberculosis doctor had an X ray plant in his surgery right at hand. Early cavities were not as a rule revealed by physical signs, it needed X rays to disclose them. The differentiation of apical from subapical lesions was of immense therapeutic importance. At Bedford Hills Sanatorium, of the patients with subclavicular lesions, 66·4 per cent. had a positive sputum against only 15 per cent. with apical lesions. Strict isolation, the backbone of tuberculosis prevention, was not indicated in 85 per cent. of apical cases, which rendered prolonged and costly institutional treatment unnecessary.

Sir HUMPHRY ROLLESTON (Cambridge) agreed that tubercle did not begin at the apex; but the term "apex" was often employed when speaking of conditions in the upper lobe. It was an interesting question whether the infraclavicular site was due to exogenous reinfection in a person who had lost his immunity from infantile infection, or an endogenous and metastatic reinfection from dormant foci, such as tuberculous glands, lying perhaps in close contact with the bronchi. Possibly both explanations were true in different cases.

Prof. A. RAMSBOTTOM (Manchester) believed the majority of apical (in the strict sense) lesions originated in childhood, and were really blood-borne. Many of the apical lesions were of bovine origin, as opposed to the subapical which were of human origin. It was extremely difficult to decide whether a case was one of apical or subapical disease, and he confessed difficulty in finding a pulmonary lesion in some of the cases in which tuberculosis had been suspected from the general symptoms and the discovery of acid-fast bacilli. He considered the so-called "abortive" tuberculous case, with bacilli found for a short time, more of a pathological fact than a clinical entity.

Dr. J. WATT (Godalming) said some of his observations conflicted with those of Dr. Fishberg. He had compared two groups of cases, apical and subapical, similar in history and clinical course; in 72 per cent. of the apical and 81 per cent. of the infraclavicular tubercle bacilli had been found at some time or other. These figures were in contrast with Dr. Fishberg's 15 and 66·4 per cent.—a complete inversion for the apical. From the sanatorium at Godalming 58 per cent. of the apical cases and 48 per cent. of the infraclavicular were discharged with disease quiescent. Practically all the new work on apical and subapical tuberculosis was, he said, based on radiography, which was not yet infallible. Apical tuberculosis was not diagnosed in this country with anything like the frequency it was in America or Germany. His own figure of 72 per cent. showed that British sanatoriums did not needlessly keep cases. He believed that: (1) the initial lesion in the adult type of phthisis occurred in diminished frequency from the lung apex (sc. above the first rib) downward; (2) in general the nearer the tuberculous lesion lay to the apex the greater the chance that it would heal.

Dr. W. BROCKBANK (Manchester) said that pulmonary tuberculosis was almost unknown among workers in lime and plaster-of-Paris, and he described special investigations made in the North-East States of U.S.A. and in Canada, from which remarkable figures of immunity had been collected.

Dr. FISHBERG, replying, said more of the apical cases would be found in private or consulting practice than in sanatoriums. In the United States they were using X rays to the utmost—they owed it to their patients. He thought the British statistics would assume a different character if every case was X rayed.

Sanocrysin Treatment.

Dr. J. R. GILLESPIE (Belfast) presided when Dr. B. R. CLARKE (Belfast) read a paper on sanocrysin treatment in pulmonary tuberculosis. Sanocrysin in a pure state, he said, was not injurious to healthy mammals in doses of 0·1–0·15 g. per kilo of body-weight; tolerance was increased by graduated dosage. The kidneys were mainly responsible for its elimination which took place more slowly than was at first supposed. It was much more liable to damage a tuberculous organ than a healthy one. In afebrile patients it was safe to begin with 0·25 g., and to increase by the same amount in arithmetical progression until 0·75 g. had been reached, which dose might then be repeated four or five times. This sequence would usually be tolerated well by patients weighing from 8 to 10 st. Over 10 st. the final dose might be increased to 1·0 g. In very light or emaciated patients 0·5 g. should be the maximum. Interval between the early doses about a week, between the larger doses 10 to 14 days. In 16 per cent. of patients treatment had to be abandoned when less than 2·0 g. had been administered; some patients could not tolerate the drug, even in smaller doses. At the end of 1928 102 patients at the Forster Green Hospital had been discharged after sanocrysin treatment. Five cases given the original large doses all showed a loss of weight varying between 1½ and 16½ lb., and developed some complication. In the remaining 97 treated by graduated doses, complications—the most serious being prolonged fever with a spread of the disease—occurred less frequently. Do not, he said, use sanocrysin unless there was a definite probability of obtaining better results with it than by conservative methods. Where sanocrysin was well tolerated, beneficial results followed in a high proportion of cases. The effect on fever cases which had not yielded to prolonged rest in bed was often very marked. For the positive sputum cases discharged from the hospital from July, 1925, to December, 1928, the after-histories were traced in the spring of 1929. Of the sanocrysin-treated, 80 per cent. of the moderate grade were alive against 63 per cent. of those not so treated; in the advanced grade, 58 per cent. of the sanocrysin-treated were alive, against 30 per cent. of the untreated. To sum up: sanocrysin was of value in two types, the early exudative cases with some resistance, and the predominantly fibroid type with symptoms and persistent tubercle bacilli in the sputum. In the exudative case he used sanocrysin as soon as possible; in the fibroid, not until sanatorium treatment had had a trial. Sanocrysin could in some cases be successfully combined with artificial pneumothorax. It was not a cure for pulmonary tuberculosis, but it was a valuable aid to treatment.

Dr. F. R. G. HEAF (Warwickshire) gave his experience of 120 positive pulmonary cases at the Warwickshire Sanatorium. He, too, had found the Danish initial doses too large. If loss of weight and rise of the sedimentation test occurred the interval between

the doses, not the doses themselves, was increased. Sanocrysin had a therapeutic value except in cases associated with toxic anæmia, cardiac and renal complications, and poor general condition, or with symptoms of enteritis. He followed the Danish dosage, increasing from 0·1 to 1·0 g. in 64 days. He specially stressed the need for attention to the weight of the patient. It was important to eliminate tubercle bacilli from the sputum before terminating sanocrysin treatment. Comparing the after-histories of 50 sanocrysin-treated patients with 50 artificial pneumothorax cases otherwise similar, the results were superior for artificial pneumothorax. Sanocrysin, for children with positive sputum, gave good results, the sputum in eight out of ten ceasing to be positive. When more time had elapsed to judge results he expected children would have proved better subjects than adults.

Dr. PETER W. EDWARDS (Cheshire) said he began to try sanocrysin two years ago, the great majority of the 37 patients treated being very advanced. The results on discharge from sanatorium were much better than he expected, 31 being definitely improved clinically and radiologically, 3 worse, and 3 dead. The cases had not been followed up.

Dr. W. STOBIE (Oxford) agreed with Dr. Clarke that the fibro-caseous type of pulmonary tuberculosis of moderate duration gave more satisfactory results, on the whole, from treatment. He agreed with Dr. Heaf that children with the adult type of phthisis occasionally did well with sanocrysin. He regarded sanocrysin as a therapeutic agent which, cautiously used, was of restricted but definite value in helping to clear up the morbid processes in certain carefully selected cases of pulmonary tuberculosis.

Prof. S. LYLE CUMMINS (Cardiff) stated that sanocrysin treatment aimed at something quite different from artificial pneumothorax and sanatorium treatment, and its value in tuberculosis had been obscured by comparisons. Although sanocrysin failed to kill tubercle bacilli in vitro, it had a marked action on tuberculous foci in vivo. He gave detailed notes on the 21 patients treated in the residential institutions of the Welsh National Memorial Association from 1925–28. Of the seven who had died, four were unsuitable for sanocrysin treatment on commencement. In other cases, whether ultimately fatal, worse, or better, in which the injections were sufficiently tolerated to allow of an adequate series of doses, a marked improvement resulted. In sanocrysin we had, he said, a means of raising the status of certain patients to a point at which they might enjoy the benefits of collapse therapy or sanatorium treatment.

Conditions Simulating Pulmonary Tuberculosis.

Dr. G. LISSANT COX (Lancashire) being in the chair the discussion was opened by Dr. F. G. CHANDLER (London). It was, he believed, by bacteriological examination of the sputum and the fæces, and by these alone, that we could establish a diagnosis of pulmonary tuberculosis or exclude it. Because of the neglect of these simple tests many cases of pulmonary tuberculosis escaped recognition in the early stages, and many non-tuberculous conditions were diagnosed as tuberculous. Examination of the fæces was necessary, because in many cases of active pulmonary tuberculosis either no expectoration was produced, apart from naso-pharyngeal mucus or muco-pus, all the pulmonary secretion being swallowed. Tubercle bacilli, if swallowed, could easily be found in the stools by the antiformin method. Since 1924 at Victoria Park Hospital the fæces had been examined as a routine when the sputum failed. Many conditions might simulate pulmonary tuberculosis, sometimes only when they were fairly advanced, as with pneumonoconiosis, sometimes only at the beginning, when symptoms (cough, sputum, bleeding) might be similar or identical; later they began to diverge and the picture became distinctive. Occasionally tuberculosis might coexist with one of the diseases by which it was simulated, such as pneumonoconiosis, lymphadenoma, syphilis, new growth, bronchiectasis, and mitral stenosis, and he instanced a number of points which would help in the diagnosis, assuming that tubercle bacilli had been found. The resemblance might be due to symptoms, such as those of fibrosis, or to the appearance of a serous pleural effusion. He enumerated the various diseases in which these occurred, giving here and there an impressionist hint at the most important points in their differentiation. The only method of distinguishing non-tuberculous from tuberculous fibrosis was to prove the absence or presence of tubercle bacilli. Pneumonoconiosis might arise from many occupations; so could anthracosis, silicosis, asbestosis, byssinosis (workers in cotton, felt, and shoddy mills). The most remarkable symptom in asbestosis was dyspnœa; in some cases asbestos fibres were found in the sputum. The introduction of iodised oil had made it possible to exclude or to localise bronchiectasis. In difficult cases the routine to follow was: a careful history, an exhaustive pathological examination, lipiodol injections, X ray examination, bronchoscopic examination. In certain cases such procedures as replacement and thoracoscopy would be needed, in others thoracotomy. He would put first the pathological examination.

Prof. F. E. TYLECOTE (Manchester) considered post-influenzal conditions should be more widely known and appreciated. There had been a tendency to smile at the suggestion he, along with others, had made that pulmonary syphilis was more common than generally believed.

Dr. W. BURTON WOOD (London) exhibited a number of slides illustrating asbestosis and pneumonoconiosis. He remarked that anthracosis has fallen into disrepute as carbon had not the effect which was believed on the lung. In asbestosis X ray films showed obliteration of the costal angles; there was a central core of asbestos fibre in the bodies in the lung. He hoped there would not be some day a claim on the State for the provision of preventorium treatment for pre-asbestos children.

Dr. P. HEFFERNAN (Derbyshire) said many persons notified as suffering from pulmonary tuberculosis were really cases of silicosis. Workers in stone tended to develop tuberculosis in later life, and the disease then generally ran a rapid course. To diagnose silicosis three things were necessary: history of exposure to silica dust, a radiogram, failure to find tubercle bacilli. He had seen a case compensated for silicosis under the special scheme; five years later the post-mortem showed the lungs free from silica; no X ray had been made. Silicosis was occasionally limited to the upper part of the lungs.

Dr. H. G. TRAYER (Baguley) believed there was a danger of attaching undue weight to the finding of an isolated positive result in a series of negatives where the clinical findings did not fit in with the presence of bacilli.

Dr. L. S. T. BURRELL (London) mentioned five conditions which resembled tuberculosis: occupational diseases arising from dust (chiefly silica) inhalation, presence in the lung of a foreign body, empyema (fibrosis at the site might be connected with a dilated bronchi and cause periodic attacks of hæmoptysis), broncho-pneumonia, pneumonia, and healed tuberculosis. The absence of tubercle bacilli from purulent sputum was strong evidence against tuberculosis. Hæmoptysis should not be taken as an indication of tuberculosis; the great majority of cases of bronchiectasis had hæmoptysis of considerable quantity.

SECTION OF OTO-RHINO-LARYNGOLOGY.

NASAL CATARRH IN CHILDREN.

Dr. DAN MCKENZIE (London), in opening a discussion on persistent nasal catarrh, especially in children, remarked that the condition was common, important, and frequently intractable. Very many of the cases were undoubtedly associated with adenoids. But

while the presence of adenoid hypertrophy often interfered with treatment he did not consider it was the cause of the condition. As R. C. Clarke had pointed out, the catarrhal child was catarrhal from the early months of life, when any appreciable hypertrophy was rare. Such children showed well the generalisation of the catarrh, bronchitis being the rule rather than otherwise. Further, catarrh was very common in adults, in whom it was most exceptional to find adenoids. An important group was certainly associated with sinus infection, with or without adenoids. Sinus infection in children was not uncommon. He placed little reliance on skiagraphy or on transillumination in excluding this condition in children. The only satisfactory method was by puncture exploration of the antra; owing to the high level of the antral floor this should be done via the middle meatus.

Apart from these there was a large class without adenoid hypertrophy or unrelieved by removal of adenoids. A general soppiness of the nasal mucosa was present with some degree of obstruction and presenting often the classical "adenoid" facies. It was important to remove large posterior ends of the inferior turbinals when dealing with adenoids, but he found this much less often needed than he had formerly thought. Such patients appeared always to have a slight cold which got worse at frequent intervals. The population as a whole seemed to be permeated with carriers. Most of us "caught a cold" about twice a year and thereby acquired immunity sufficient to last for some six months. The catarrhal patient did not get sufficient immunity. This was the class that was difficult to treat. He relied more and more on general measures aimed at improving the health and building up resistance. But here he felt impelled to utter a protest against the extremist tendency everywhere noticeable. Not content with exposing themselves, the protagonists of the "back to nature" school subjected their children to the same régime. A shivering miserable child with running eyes and nose and purple skin was an object for profound pity. We could not afford to ignore the many generations that separated us from savagery, and to attempt to return to nudity defeated its own object. Many of us could not stand this intensive hardening, which was by no means the modern method some of its advocates supposed. It was related of one Aristides that having a catarrh he sought the advice of the oracle; the god told him to smear himself with mud and run thrice round the temple. In spite of bitter weather he did so, and was rewarded by a warm glow and health. But his companion who attempted the same treatment suffered a paralytic spasm and was hardly restored to life. So too with modern patients, a too rigorous disregard of east winds might not merely fail in promoting health, but prove actually disastrous.

Mr. F. P. GILHESPY (Birmingham) said he had recently examined 50 consecutive cases of chronic nasal catarrh in children attending a school clinic. He divided them into five groups:—

(*a*) Previous tonsil and adenoid operation: Present antral disease, 23.

(*b*) No previous operation, no adenoids: Present antral disease, 9.

(*c*) Previous tonsil and adenoid operation: No antral disease, 10.

(*d*) Previous tonsil and adenoid operation incomplete, 6.

(*e*) Atrophic rhinitis, 2.

The criterion of antral disease was in each case naked-eye pus or muco-pus in the syringe washing. In most of the cases pus had been present in the nose. The presence of adenoids interfered with the treatment of the antral disease. For the latter, except when acute, he thought repeated lavage of little value; a pernasal antrostomy was needed. In 32 of the 50 cases examined there was antral disease and none of these had adenoids; absence or removal of adenoids was not in itself enough to secure recovery of the sinusitis. In the third category were ten children without sinus disease whose catarrh persisted despite removal of adenoids. This constituted the true "catarrhal" group. Treatment must be along general lines, during which ultra-violet therapy proved valuable.

Mr. DOUGLAS GUTHRIE (Edinburgh) recognised two varieties of adenoid hypertrophy. A central mass was common; less frequently one found a diffuse sheet of adenoid tissue, and in these cases nasal discharge rather than obstruction was likely to be present. Another common cause of chronic rhinitis in Edinburgh was diphtheritic infection. Sinus disease accounted for a third group. Finally, there was a class of cases in which infection persisted in a narrow nose, following a series of acute colds. For this type it was necessary to restore the patency of the nasal passages by conchotomy or a septum operation. Although he did not like such operations in the young he often felt it was necessary to do them, and if one was careful no arrest of nasal development need occur. Further measures were cleansing of the nasal passages by means of suction and oily applications. Diastolisation was valuable; by means of a rubber bag the mucosa was subjected to massage. General measures should include diet, ultra-violet therapy, and large doses of sodium bicarbonate. Properly supervised breathing exercises were important. Ionisation he regarded as impracticable in children and vaccines as useless.

Dr. T. C. GRAVES (Birmingham) remarked on the great importance of treating chronic nasal discharge. Among insane adults one-third had chronic rhinitis. He instanced six adult cases in which treatment of the nasal infection was followed by recovery from (certified) insanity.

Dr. P. WATSON-WILLIAMS (Bristol) said the great majority of cases were caused by either adenoids or sinus disease or both. Sinus disease was much more frequent in young children than many supposed who did not make systematic search for it. When the antra are healthy the sphenoidal or ethmoidal cells should be examined. This could be done in even quite young children.

Tuberculosis of the Larynx.

In opening a joint discussion with the Section of Tuberculosis Mr. W. G. HOWARTH (London) said that laryngeal abnormality was present in 10 per cent. of all hospital cases of pulmonary tuberculosis. This might be:—

(*a*) Anæmia of the mucosa, part of a general anæmia.

(*b*) Interarytenoid hypertrophy, not necessarily tuberculous.

(*c*) Tuberculous laryngitis.

The incidence varied considerably with the class of case. He had found it in 8 per cent. of sanatorium patients, in 4 per cent. of the patients attending the Chest Hospital. At the State Sanatorium, New Jersey, 25 per cent. of the patients were affected. Very rarely one might find a primary tuberculoma of the larynx. It occurred in elderly persons and was apt to be mistaken for cancer. But almost always the laryngeal condition was secondary to pulmonary disease. The original infection occurred through the mucous membrane; secondary submucous lymphatic spread subsequently took place. Most commonly the posterior half of the larynx was affected. But the lesion could occur anywhere, and when in an unusual situation diagnosis might be difficult. As examples of anomalous appearances he cited a gelatinous infiltration of the whole of one vocal cord or a diffuse symptomless subglottic infiltration. Many unusual appearances of the larynx were eventually shown to be tuberculous.

In addition to the common symptoms of hoarseness or dysphagia he would direct attention to three early signs: (1) a voice easily tired; (2) sudden and intermittent disturbances of phonation; (3) tickling or

dryness of the throat. Early diagnosis was of the very greatest importance for the sake of treatment. Treatment should be primarily general, as the pulmonary lesion was the important one. Local treatment consisted in: (1) absolute voice rest; (2) galvano-cautery in selected cases. With voice rest even very large lesions might heal completely; it might need to be continued for as much as six months and the patients required constant encouragement. The cautery was valuable in carefully selected cases; it did not destroy the actual lesions, but acted as a counter-irritant. He had had little experience of direct sunlight treatment of the larynx, but found that the dose required very careful regulation. With artificial sunlight the treatment was lengthy, and he doubted whether a corresponding advantage was secured. In rare cases where the lung condition was inactive and the laryngeal progressive a tracheotomy might secure the complete rest of the larynx that was essential. In the later stages treatment should be symptomatic and directed to relief of cough and of pain. For the latter he relied on insufflations, and had been disappointed with nerve-blocking injections.

Sir StClair Thomson (London) recalled that one case in every three of phthisis suffered from a laryngeal complication, and estimated that 55,000 such sufferers existed to-day in England. Fortunately not only was phthisis becoming more rare, but the incidence of laryngeal tubercle was also declining. Formerly males had been more affected, but since the entry of women into the labour market the sex difference had largely disappeared. The more advanced the pulmonary disease the greater the incidence of laryngeal lesions. Further, the presence of a laryngeal complication was of great prognostic significance. Of the cases from a sanatorium without laryngeal tubercle two-thirds were alive ten years later; of those with laryngeal tubercle only one-third survived ten years. The difference was most pronounced among the early cases. When a laryngeal complication occurred during sanatorium life it was of grave significance. Of cases treated by silence alone the larynx was cured in one-third and improved in one-third. Among the rare cases selected for cauterisation 62 per cent. were cured. Of all sanatorium patients one-fourth were cured.

Mr. H. Morriston Davies (Ruthin) emphasised the importance of routine examination, even in cases of phthisis with no laryngeal symptoms. The presence of laryngeal tubercle was of material significance where operative treatment for the lung was under consideration. Healed laryngeal tubercle, if attended with much deformity, so that a good cough could not be produced, was a contra-indication for artificial pneumothorax. On the other hand, the presence of a laryngeal complication might determine one to do a pneumothorax operation, where without it one would not. Though of less significance where phrenic avulsion was contemplated the condition of the larynx needed even greater regard when a thoracoplasty was under consideration.

Sir James Dundas-Grant (London) pointed out that in cases of doubt a biopsy presented great advantages, especially where a thyrotomy might be contemplated. He relied on galvano-cautery for many cases of laryngeal tubercle, and thought pain especially was a pressing indication.

Mr. R. Scott Stevenson (London) had seen cases in which careful clinical and radiological examination failed to reveal any pulmonary tubercle, but where there was advanced laryngeal disease. Laryngoscopy was therefore important with any obscure chest condition.

Dr. S. Moritz (Manchester) emphasised the importance of using the galvano-cautery to effect deep punctures, to produce fibrosis, and not superficially. He referred to the difficulties presented by the simultaneous occurrence of syphilis and tubercle in the larynx.

Reviews and Notices of Books.

Stone in the Urinary Tract.

By H. P. Winsbury White, M.B., Ch.B. Edin., F.R.C.S., Assistant Urological Surgeon, St. Paul's Hospital. London: J. and A. Churchill. 1929. Pp. 344. 35*s*.

Close upon Mr. Swift Joly's recently published work on "Calculus" comes another treatise on the same disease by Mr. Winsbury White. The ground covered is the same, but the subject is treated differently. Whereas Mr. Swift Joly produced a monograph for the expert Mr. Winsbury White caters for the practitioner and for the general surgeon who deals occasionally with cases of stone. For this reason such matters as the ætiology of calculus formation are dealt with less fully in the book now under review, and more space is devoted to such practical points as lithiasis in pregnancy and in children. This addition will be appreciated by the expert as well as those for whom the book has been more particularly written. But as a matter of fact the book contains a vast amount of information interesting to all genito-urinary surgeons. The only criticisms we would offer are that (1) the arrangement of the subject matter is somewhat haphazard; when the book is used for reference it is difficult to find information without first consulting the index; (2) the important points in the treatment of stone do not receive enough emphasis at the expense of unessentials. The plates are excellent and are more numerous than is usual in a work published this side of the Atlantic. The bibliography at the end of the book is excellent. The author has searched out the literature of stone from the years 1910–28 so that those who require information not found in the text may know where to obtain it.

Orthopædic Surgery.

Second edition, revised. By Sir Robert Jones, Bart., K.B.E., C.B., F.R.C.S., F.A.C.S., and Robert W. Lovett, M.D., F.A.C.S. With the collaboration of Nathaniel Allison, M.D., F.A.C.S., Frank R. Ober, M.D., and Harry Platt, M.D., M.S., F.R.C.S. London: Humphrey Milford. Oxford University Press. 1929. Pp. 807. £2 12*s*. 6*d*.

In the interval of six years since we welcomed the first edition of this work the untimely death of Dr. R. W. Lovett, of Boston, has put an end to a fertile collaboration. Sir Robert Jones has wisely sought the help of two well-known orthopædic surgeons of Boston and of Mr. Harry Platt, of Manchester. The work has been brought thoroughly up to date, and the omissions which we called attention to in our former notice have been remedied. The excisions of obsolete matter have not balanced the additions, and the book is more than a hundred pages larger than it was. The number of figures has also been increased. Otherwise there is no great change in the book, nor is any revolution in treatment recorded. Scoliosis, which was a subject that the late Dr. Lovett made peculiarly his own, is dealt with at greater length than before, and details of new methods of applying plaster jackets are described. The sound, conservative opinions expressed in the first edition on arthroplasty of the knee, and the treatment of Pott's disease and scoliosis by bone-grafts or the methods associated with the name of Russell Hibbs, of New York, are repeated. The subject of backache or low back pain, as the Americans prefer to call it, is still discussed cautiously; the waves of enthusiastic surgery based on supposed subluxations, minor bone injuries, and abnormalities of development of the spine, seem to spend their energy before they reach these shores. The chapter on Volkmann's ischæmic paralysis is a valuable addition, and fills a gap which was left in the first edition. That on acute osteo-

myelitis is of notable value, and follows to a great extent the lines of the discussion in the Orthopædic Section of the Royal Society of Medicine last year. Fractures are dealt with at greater length in this edition, and this will especially enhance the value of the work to the practitioner who is not concerned with the more specialised branches of orthopædics.

PRINCIPLES AND PRACTICE OF MINOR SURGERY.

Sixth edition. By EDWARD MILTON FOOTE, A.M., M.D., Visiting Surgeon, St. Joseph's Hospital, &c.; and EDWARD MEAKIN LIVINGSTONE, B.Sc., M.D., Assistant Visiting Surgeon, Bellevue Hospital. London and New York: D. Appleton and Company. 1929. Pp. 787. 35*s*.

THIS work presents the principles and practice of minor surgery in all its branches in a logical, scientific, and readable manner. It is divided into three parts—minor surgical technique, the principles of diagnosis and treatment, and the practice of minor surgery. The author's interpretation of "minor" surgery is almost too liberal, for the volume includes consideration of every surgical procedure, outside the abdomen, with which the practitioner could legitimately be called on to deal. Details of the pathology and treatment of surgical conditions, as grave as rupture of the urethra, loose bodies in the knee-joint, or the operation of colostomy are given; yet there is no mention of appendicitis or of perforation of gastric or duodenal ulcers. Apart from such curious regional limitation the volume should prove invaluable to the practitioner, who is called on to deal with surgical cases and to the young surgeon. The teaching is quite modern and at the same time sound and practical. The majority of the illustrations are beautifully reproduced photographs.

ENDOCRINOLOGY AND ORGANOTHERAPY.

Diseases of the Thyroid Gland. Second edition. By A. E. HERTZLER, M.D., Surgeon to the Halstead Hospital, Kansas. London: Henry Kimpton. 1929. Pp. 286. 32*s*.

IN this new edition the result of a continuation of Dr. Hertzler's studies on the pathology of goitre and thyrotoxic conditions is presented. There are also included chapters dealing with the management of goitre patients and the technique of thyroid surgery, but the author's views on the pathology of these diseases are the chief point of interest. The most usually accepted classification of goitres divides them up into colloid goitres, adenomas without toxic symptoms, adenomas with toxic symptoms, and Graves's disease or true exopnthalmic goitre. Dr. Hertzler holds that these groups do not represent separate diseases, but merely stages for the most part of one progressive disease. The same individual may run the gamut of the whole series. The colloid goitres are smooth in outline and the patient has no constitutional symptoms; their beginning depends on a uniform increase of colloid within the acini resulting in the homogeneous enlargement of the whole gland. This is the early stage. After a time new acini appear, adding their part to the increase in size of the gland; with their continued development the thyroid becomes irregular or bosselated. These are the glands which some authors call "adenomas." Hertzler believes that they are not truly "adenomatous," and he would reserve the term adenoma for the true benign tumours or fœtal adenomas. The latter develop from a single nodule and are isolated, encapsulated, and completely surrounded by the substance of normal thyroid on which they rest, but are independent of it in structure and growth. He suggests that the confusion in terminology is due to the failure to distinguish between the bosselations of an old colloid goitre and the fœtal adenomas. The clinical significance of these two varieties is entirely different. Hertzler holds further that the bosselated colloid goitres sooner or later become toxic, generally after about 16 years. The fœtal adenomas are not subject to the periodic progressions and recessions of the bosselated goitres and grow gradually. They may degenerate and form cysts or they may become malignant; sometimes they become mildly toxic, but this is comparatively rare. Finally, he would differentiate true Graves's disease from the toxic bosselated goitres. In true Graves's disease it is the proliferation of the epithelium of the original acini which is the characteristic feature, while in the toxic bosselated goitres the toxicity is due to the proliferation of acini developing in the interstitial cells.

These views require careful consideration, and their presentation in the present volume is clear and concise.

Organhormone und Organtherapie. By Prof. AUGUST BIER and others. Munich: J. F. Lehmanns. 1929. Pp. 91. M. 4.50.

THE principal thesis of this little book, which is made up of reprints from the *Münchener Medizinische Wochenschrift*, is that, since organs normally regenerate and give rise to substances which preserve the normal physiological balance, it should be possible to approach something like regeneration or at least re-established function by the administration of preparations of appropriate organs in cases of disturbed structure or function. This conception is, of course, being widely applied in many directions, but those followed in this book merit special attention, because a measure of success claimed by so distinguished an authority as Prof. Bier cannot be ignored. The book is divided into four parts. In the first Prof. Bier deals with the general principles of organotherapy and in particular with the work of his pupils, set out in the succeeding sections. The second part consists of a discussion of diseases of the liver and bile passages which have been treated by various extracts of liver, gall-bladder mucosa, and extrahepatic accessory glands. The substance chiefly used was choloton, and the authors frankly state that they are concerned with the clinical effectivity of the preparation and not with its mechanism of action. Cases of many varieties of liver and gall-bladder diseases have been treated with an improvement of symptoms (jaundice, pain, rigors, enlargement of liver, &c.) which impressed the observers. In the third part the treatment of tabes, progressive paralysis, and multiple sclerosis with a complex preparation of nervous tissue, vitamins, calcium, iron, and carbohydrate is described. This preparation is called Promonta, and is prepared in the cold on the principle of keeping the nerve substance unchanged. Treatment by the mouth with this substance combined with strychnine nitrate is said to have produced extraordinary symptomatic improvement. The last and shortest part deals with the treatment of Graves's disease by injection of animal blood. Sterile defibrinated ram's and calf's bloods were used, 5 c.cm. doses being injected intramuscularly at eight-day intervals. Anaphylaxis is obviated by using the different animals' bloods alternately, two to four injections being generally sufficient to produce a distinct improvement in symptoms. It is claimed by the authors that it is not merely the febrile reaction which determines the degree of improvement, but some more fundamentally important process. Time and large numbers of controlled cases only can decide on the reliability of these findings. The principles involved are vague, but the book is commendable in so far as it insists on a broader physiological outlook and gives many useful suggestions for further research.

Die Pathogenetischen Grundlagen der Thyreotoxicosetherapie. By JOHAN HOLST. Oslo: I. Kommisjon Hos Jacob Dybwad. 1928. Pp. 176.

THE introduction of iodine into the treatment of exophthalmic goitre has during the last few years given results which opened a new chapter in our knowledge of the diseases of the thyroid gland. It is

quite clear that the theoretical basis for such a treatment is something totally different from that of the treatment of endemic goitre by iodine salts; for, whereas the latter is now well established as due to a deficiency of iodine, the former is associated rather with a flooding of the tissues with the active principles of the thyroid which are certainly in some way combined with iodine. Holst's work presents a definite advance in the direction of explaining this apparent paradox. He examines the problem by chemical, histological, and clinical methods. Administration of iodine (Plummer's method) in Graves's disease is followed by a rapid clinical improvement, fall in metabolic rate, and an increase in stored colloid in the gland itself. Analysis of the blood for iodine shows that this substance occurs in two main forms, one inorganic and alcohol soluble and the other organic, alcohol insoluble, and associated with protein. Both these fractions are much increased in thyrotoxic conditions. Treatment with iodine produces the effect of very largely increasing the inorganic fraction in the blood but of diminishing the organic to almost normal. Taking this in conjunction with the other observed effects of iodine Holst puts forward the view that the thyrotoxic condition is due to the flooding of the tissues with the active secretion of the thyroid, that this active secretion is identical with the organically combined iodine in the blood, and that the controlling factor is inorganic iodine in the blood. No information is given about the factor which gives rise to the so-called thyroid diarrhœa, for the high inorganic iodine in the blood cannot be the controlling factor normally. Throughout the book no mention is made of other glands which certainly have to do with the normal endocrine balance. Dr. Holst pays careful attention to the selection of the best period for operation after the preliminary iodine treatment, and to the fact that if this period is missed thyrotoxic symptoms again supervene as a result of hyperiodism. Emphasis is laid on the danger of intermittent treatment; once treatment with iodine is begun it should only be discontinued for operation. Clearly this treatment is not yet suitable for application in general practice. Its main value lies in so diminishing the thyrotoxic symptoms that operation can be safely undertaken. Continued treatment after operation with small doses of iodine has in Holst's cases yielded good results.

The book is well worth studying because it is written by one who is both an endocrinologist and a surgeon. It is written in pleasant style, easy to follow, and the diagrams are excellent.

DIAGNOSTIC METHODS.

Diagnostic Methods and Interpretations in Internal Medicine. By SAMUEL A. LOEWENBERG, M.D., F.A.C.P., Assistant Professor of Clinical Medicine, Jefferson Medical College. Philadelphia: F. A. Davis Company. 1929. Pp. 1032.

THIS book has a wide scope, for the author's aim is to cover the field of diagnosis in medicine. The chapters devoted to the circulatory and respiratory systems are adequately dealt with and physical examination is lucidly explained; the examination of the abdominal viscera is not so well described, while the section on the endocrines suggests rather the small booklets thrust upon practitioners by commercial firms—for example, a differential table is given to distinguish between pineal and thymus hyper function. That such tables, which have no scientific foundation, should be incorporated and a method of such diagnostic value as the use of lipiodol omitted detracts greatly from the value of the book. The author likes differential tables, although the ones supplied are not of much diagnostic value. One table given is that of the differential points between "gall duct" (this term is new to us and its significance uncertain), "gastric ulcer," and "pyloric spasm." According to this table application of cold is supposed to ease the pain in gastric ulcer and to intensify it in pyloric spasm; this is not our experience. There are several omissions—for example, the reticulocytes are not mentioned in connexion with pernicious anæmia nor are Froin's syndrome and the protein content of the C.S.F. in the examination of the cerebro-spinal fluid. The photographs are numerous; many are good, others such as that showing the difficulties of percussion of the heart in the "extremely modest," are quite unnecessary. A photograph of the technique of entering a vein is given showing the operator equipped with a rubber glove, syringe in hand, piercing the dusky skin. The outcome of a close study of this work is that the task of writing a comprehensive book on diagnostic medicine is too heavy a task in modern times. If the author had confined himself to a monograph on the diagnosis of respiratory and circulatory diseases alone he would have achieved more success.

CLINICAL ELECTROCARDIOGRAMS.

Their Interpretation and Significance. By FREDERICK A. WILLIUS, B.S., M.D., M.S., The Mayo Clinic, Rochester, Minnesota. London and Philadelphia: W. B. Saunders Company. 1929. Pp. 219. 36*s*.

THIS book consists essentially of a large collection of electrocardiograms illustrating the various abnormalities which occur in different pathological conditions. Many of these records are interesting, and some are rare, as, for example, those given in the last chapter, which deals with the dying human heart. At least 50 per cent. of the records might have been omitted with advantage, for although good in themselves they are redundant; the remainder would have amply sufficed to illustrate all the points to which the author refers. Apart from a few tables dealing with mortality statistics, the text is of a most elementary character, and falls far below the standard of what might reasonably be expected in a book dealing with such a technical subject. Each chapter is followed by a comprehensive list of references, but these are unselected, and few of the papers to which they refer are even mentioned in the text.

JOURNALS.

JOURNAL OF INDUSTRIAL HYGIENE, September.—This issue is devoted to three papers, each concerned with some form of tuberculosis in industry. In the first B. S. Coleman points out how industry groups the adult community in a way which is convenient for fighting tuberculosis. By medical examinations on engagement, and supervision during employment, the tuberculous can be detected early and their fellows protected from contact infection, whilst industry can also provide for the convalescent that remunerative occupation which is so advantageous to cure.—In the second paper E. R. Hayhurst and his colleagues describe exposure to silica dust in a sandstone quarry in Ohio, where, notwithstanding the presence in the stone of some 95 per cent. silica, the death-rate from pulmonary tuberculosis is low. The evidence of this low mortality, based on statistics, is supported by the result of a careful medical examination of over 900 workmen. Illustrations are given which leave no doubt about the presence of a dust hazard at the quarry, and the puzzle is why the silica dust does not produce its usual effect. A clue may lie in the matrix or bond which holds the silica crystals together; it forms 3 to 8 per cent. of the mass and is composed of ankerite (carbonates of calcium, magnesium, and ferrous iron). At present, however, no other comparable instance can be quoted.—The last paper is by D. E. Cummings, who deals with the separation of particulate matter smaller than screen sizes into graded fractions. He describes a method by which dust particles can be accurately separated one from the other according to size. This method may be of value in preparing material for inhalation experiments. The article is one of a series of studies of experimental pneumonoconiosis.

THE LANCET.

LONDON: SATURDAY, OCTOBER 12, 1929.

THE FUTURE OF VACCINE THERAPY.

THE modern practice of vaccine therapy rests in effect less on any theory of immunity than on JENNER'S success in protecting from subsequent infection with small-pox those who had been vaccinated with material from cow-pox. Indeed, the word vaccine introduced to describe this specific virus is now used in ampler connotation to cover any virus or bacterial body, even any foreign protein, which evokes a response when introduced into an animal body by inoculation. A vaccine has come to be almost synonymous with an antigen. It was PASTEUR who saw in JENNER'S results the germ of a law of general validity—namely, that by causing an animal or inoculated person to undergo successfully a mild infection, protection is thereby obtained from a more severe infection of the same nature brought about naturally or artificially. The results of such active immunisation are essentially protective, and are specific for the virus inoculated. They are limited in applicability when a living virus is used, owing to the difficulty of finding one whose potency is naturally reduced, so that as a rule artificial ways of reducing the virulence must be adopted. Active immunisation by such attenuated viruses is used successfully in the treatment of rabies, and forms the foundation of the methods of producing immune sera in animals.

For use in man any virus, however attenuated, which is still able to propagate itself and thus increase in the site of inoculation or spread throughout the body is dangerous. Bacteria for vaccines in human therapy are therefore at least killed, usually by heat; the bacterial bodies may even be disintegrated chemically, as in detoxicated vaccines. Experiments with such bacterial vaccines, sometimes together with their soluble toxins, have been made in the treatment of human infections for a generation, but so far no therapeutic principles have been evolved that have received general acceptance. The choice of patients suitable for vaccine treatment, the methods of preparing the vaccinal material and of administering it, and the results that may reasonably be expected, even the successes claimed for vaccine therapy, are still debated. Certain facts have, however, accumulated. The body responds to any parenteral introduction of foreign protein by a reaction which may be so violent as to constitute shock, with profound effect on the nervous system, the circulation, and the heat-regulating mechanism. The reaction may be a local one, limited to the site of inoculation, and sometimes a focal one at the site of infection. On the other hand, there may be no apparent reaction. A consideration of experimental work on animals, and of the methods used in fighting animal diseases on a large scale, throws some light on the way vaccines work in therapeutics, if it be granted that the presence of antibodies in the blood gives an indication of the degree of immunity obtained, a proposition not yet established. In animals inoculation, especially intravenous inoculation, on three or four successive days produces a serum with high but evanescent content of antibodies. Vaccines at intervals of some weeks give sera with antibody of long duration. ALMROTH WRIGHT'S opsonic work led to vaccine administration at intervals of several days to avoid a possible negative phase, and to the use of small doses of vaccinal material; his careful immunisation experiments were carried out with the control of the opsonic index. Since this method has lapsed into disuse, no real control is made in vaccine therapy applied to man, except that to avoid active and immediate harm to the patient. Under rather than overdosage is the rule. The tendency, too, is to use less often the bacteria cultivated from the individual, and to depend rather upon stock vaccines. Indeed the specificity of the vaccine employed may be disregarded, as in the use of typhoid stock vaccine for many conditions. Substances other than bacterial bodies may be used, and vaccine therapy then becomes frankly a non-specific protein therapy, the dosage and results being decided empirically. Many laboratory workers refuse to see in the use of vaccines anything more than a specific protection against a reinfection. Pathologists, however, working in close touch with clinicians and with the patient, seem to advocate vaccine treatment in a great number of infective processes. Meanwhile, the practitioner is in a quandary, swayed to and fro by his inadequately controlled clinical impressions, and yet hesitating to omit from his means of treatment anything that is likely to benefit his patient.

Theoretically it should be possible to divide cases of infective diseases into three groups. In the first the patient is doing well, the infecting forces are being dealt with adequately by the natural resistance, and no anxiety about the outcome need be felt. In the second group the infection is localised, but there is a state of unstable equilibrium between the resistance of the patient and the infection which at any time may be upset. Thirdly, there is the group in which the patient is doing badly and is being overwhelmed by the infection. The first group obviously needs no specific treatment in order to ensure recovery. In the third group a procedure bringing about further toxic effects is not to be contemplated lightly, and adding more poison may be actively harmful. It is probable that in the developments of the new chemotherapy there will be found a better means of treatment for such cases. It is only in the second group, where there is already some degree of resistance, that the possibility of stimulating that resistance and calling up further antibodies to the infecting germs by injecting vaccines should be considered. (In hydrophobia immunising treatment is begun after infection takes place, and completed before symptoms of the disease show themselves; but this is essentially prophylactic treatment, which is not now under discussion.) In this group of cases, where symptoms have already appeared but progress is delayed and resistance is inadequate, or is liable to break down at any time, medical vaccine therapy is largely used in practice, and the success of this method of treatment has been assessed differently by various observers. The scientific basis for it has not been demonstrated; the advocates of vaccines in treatment base their claims upon the evidence obtained by clinical judgment. Evidence in support from the experimental side is wanting, but this may well be due to the fact that investigators of the problems of immunity have been working on other lines. Even the

site of antibody formation is still largely a matter of conjecture, and the whole problem of immunity has changed its aspect many times within the last 30 years and is still quite unstable. The nebulous views of resistance to infection held by earlier pathologists were succeeded by the coördinated idea of phagocytosis established by METCHNIKOFF. In its original form the phagocytic properties of the wandering white cells of the blood were regarded as the means by which the body dealt with infecting bacteria. With the extension that the fixed cells of the lymphatics, connective tissues, and endothelium also exhibit phagocytic and thus protective properties, METCHNIKOFF'S idea remains the basic principle of the theory of immunity of the present day. EHRLICH introduced another idea, that the humours of the blood and body fluids carried antibodies of various kinds, which either were antibacterial and antitoxic in themselves, or stimulated the phagocytes and prepared the bacteria for ingestion. These antibodies were represented as actual substances in the blood. The theory was amplified to include any new phenomena observed, and at last became a maze of incomprehensibly involved patterns. A simplification followed, and M. NICOLLE saw in the immunity processes alternative phases of coagulation and lysis. Now recent advances in physical chemistry show that colloids are susceptible of precipitation by electrolytes, and that one colloid may act on another sometimes in a protective or stabilising way, sometimes sensitising it, so that it becomes more easily precipitated. According to this physicochemical theory the changing conditions of the colloids of the blood and tissues are responsible for the phenomena observed in the process of immunisation, and there are not various antibody substances in the blood of an immunised animal, but phases of one immune reaction. This may be an over-simplification. Certainly in this theory there seems little room for specificity; whereas the immunity response consists essentially of a highly specific action combined with a non-specific general reaction. No satisfying explanation is yet forthcoming of the curious mixture of resistance and sensitiveness that occurs in immunity. Lately, too, our ideas on the variation of bacteria, not only in virulence but even in physical characters and appearance in cultures, have undergone considerable extension. Much ground remains to be covered, therefore, before a satisfactory basis for the use of vaccines in the treatment of infection can be reached. It is the time neither for complacent scepticism nor for violent advocacy, but for open-minded discussion that will stimulate further research.

THE MECHANISM OF COMPENSATION FOR SILICOSIS.

EACH new step in granting compensation for disability due to occupation seems to require new procedure. If disability is due to an accident, the workman carries a disputed claim into court, where after medical, as well as other, evidence has been heard the issue is decided. If a scheduled disease is concerned, medical evidence is heard and assessed by a medical referee, whose decision is final. In recent years compensation has been granted for a disease—silicosis—in connexion with which existing procedure is inapplicable. Schemes have been tried out in the small refractories industry during the past ten years; but in the last 12 months compensation has been granted widely, so as to cover practically all industries in which a silica-dust hazard exists. These industries include the getting and use of sandstone, whether for road metal, building, monumental masonry, or grinding metals; the production and use of powdered flint, whether in the pottery trade or for the making of silica paints, abrasive soaps or vitreous enamels; and the fracture of quartz and quartzite in the granite industry or in the process of tin mining. This extension enlarges the scope of compensation for silicosis from some 3000 workmen to a large population, of which the size is uncertain; but it numbers anything from 50,000 to 100,000. This population is scattered all over the country, but is more densely grouped in certain industrial areas, such as the gritstone district of Derbyshire, the pottery towns of Staffordshire, and the cutlery centre at Sheffield. The problem to be faced differs from that tackled with such success in the gold-mining industry on the Rand, where only about 10,000 European miners are employed, both in the numbers concerned and their wide distribution over many varied industries.

A departmental committee, under the chairmanship of Dr. J. C. BRIDGE, senior medical inspector of factories, was appointed in December of last year to consider what medical arrangements should be made to cope with the situation. Their report[1] has just been issued. They envisage plans in which the medical services required for controlling the occurrence of the disease, such as examination on engagement and periodically thereafter, are combined with those needed for diagnosing the disease for compensation purposes. The final recommendations of the committee are modelled on the scheme which has achieved success in South Africa, modified to meet our more complicated conditions. They include the creation at different centres of medical boards, each consisting of not less than two whole-time experts, who will visit factories, quarries, and mines to carry out their duties, which may be greatly facilitated in country places by the use of efficient mobile X ray apparatus. It is proposed that a chief medical officer should be appointed to coördinate and standardise the work of all the boards; he would reside at a central bureau, probably at Sheffield, where research would be organised and pursued. The expenses involved are to be borne by the industries concerned, which will contribute to form a joint general compensation fund, as the refractories and sandstone industries have already done. The wisdom of adopting this South African precedent is seen by referring to the latest report from the Rand,[2] which tells how the production-rate of simple silicosis on the Rand is now declining year by year in an entirely satisfactory way. It tells also how this has resulted from minimising, first, the dust hazard, and then exposure to tuberculous infection; and how action has throughout been based upon and checked by exact information disclosed by the Medical Bureau. It tells, in fact, how that preventable associate of tuberculosis—silicosis—can be combated. How great an influence would be exerted upon the prevalence of tuberculosis in Great Britain by the elimination of silicosis can hardly be guessed; but the committee hold silicosis to be far more widespread than is generally admitted. If it is really found to occur in industries and occupations where heretofore its presence has not been suspected, the effect of its control on the incidence of tuberculosis in this country should be considerable.

[1] Report of Silicosis (Medical Arrangements) Committee. London: H.M. Stationery Office. 1929. 6d.

[2] Report of Miners' Phthisis Medical Bureau for year ended July 31st, 1928. Pretoria: The Government Printer. 1929. 6s.

THE DIAGNOSIS OF DISEASE OF THE NASAL SINUSES.

As a rule there is no difficulty in recognising frank suppuration in a nasal accessory sinus, although when several cavities are involved the presence of disease in one of them may be overlooked. But when the discharge is mucoid and scanty, as in the cases formerly called latent, it is often by no means easy to diagnose the presence of pus or to determine which sinus or sinuses are affected. Here radiography is of great service, but is also subject to error, one cause of which is that past disease leaves changes which are represented on the radiogram, and may be indistinguishable from the signs of present inflammation. In the course of the routine examination of asthmatics at the Hospital of the University of Pennsylvania, R. A. KERN and H. P. SCHENK[1] were impressed by the frequent discrepancies between the findings of the rhinologist and the radiologist, and by the fact that such discrepancies were sometimes due to proven error on the part of one or other of these methods of examination. Accordingly, they subjected a series of 200 asthmatics, first to a clinical, and then to a radiological examination of the nasal sinuses, and finally, wherever possible, to an operative investigation. They also had the same examination carried out in a control group of 50 "normal" people, who showed no obvious sign of respiratory disease and no history of sinus disease in the past. Both clinical and radiographic examinations were carried out in a thorough manner, an essential part of the former being the routine use of the nasopharyngoscope. The clinical investigation included irrigation when it seemed necessary, but not a bacteriological or cytological examination of the washings.

Antrum washings, the writers hold, will be returned clear in the presence of antral polyps, thickened diseased mucosa, or inspissated secretion, and hence that the return of clear fluid by no means shows for certain that the cavity is healthy. In this connexion a bacteriological examination of the washings is very helpful; a profuse growth of a pathogenic organism is doubtless proof of the infected state of the sinus, but we think that further research is necessary before it can be accepted that the finding of a few organisms in an otherwise apparently healthy sinus is definite evidence of disease. In the present investigation KERN and SCHENK believe that the large percentage of error shown by clinical and radiographic examination of the maxillary sinus arose because the rhinologist based his diagnosis of "normal sinus" on the return of clear fluid on irrigation. Their conclusions on the results in general may be stated shortly. Neither clinical nor radiographic examination is always reliable, but of the two, radiography is the more sensitive, especially in the study of the ethmoidal and sphenoidal sinuses. Radiography picks up the evidence of past as well as present disease, so a positive finding does not necessarily mean clinically active disease; also, it often overlooks recent acute infection, whereas clinical examination is more apt to overlook chronic disease, especially of the posterior sinuses. Under transillumination past disease, or normal thick bone, may be mistaken for active disease, and, on the other hand, polypi or mucoid secretion may transmit light normally; both clinical and radiographic methods should, therefore, be employed, neither being relied on alone. KERN and SCHENK consider that in asthmatics a positive finding by either method not only justifies, but indicates opening of the sinus suspected. A very high incidence of sinus disease (80·5 per cent.) was found by radiography in their series of asthmatics, while clinical methods showed 67 per cent. But the incidence was also very high in the control "normal" group, 72 per cent. being diagnosed by radiography as having one or more infected sinuses, and 26 per cent. by clinical examination. This group was not, of course, examined by operative methods.

These figures may be taken to show that inflammation in the nasal sinuses produces permanent change which is demonstrated by radiography, and it also shows that affections of the sinuses are very common in the neighbourhood of Philadelphia. So far as we know, no data are available on the incidence of sinus disease among so-called "normals" in this country. This might usefully be investigated. Sinus infection has, however, been recognised as an important cause of chronic nasal catarrh in children, a view set out by Dr. DAN MCKENZIE in the course of a discussion summarised on p. 772. He places little reliance on skiagraphy or on transillumination in excluding this condition in children, relying rather on puncture when the maxillary antra come under suspicion. Contributing to the same discussion, Dr. P. WATSON-WILLIAMS remarked that the sphenoidal and ethmoidal cells should be examined in even quite young children. For the treatment of antral disease in children, Mr. F. P. GILLESPY considered a pernasal antrostomy the appropriate method, and this method is also advocated by Mr. HAROLD BARWELL in a paper recently read before the Section of Laryngology of the Royal Society of Medicine.[2]

[1] Amer. Jour. Med. Sci., August, 1929, p. 168.

[2] Journal of Laryngology, October, 1929, p. 674.

Annotations.

"Ne quid nimis."

THE SALE OF ARSENIC.

"THE unrestricted sale of arsenic," declared Parliament in 1851, "facilitates the commission of crime." This incontestable declaration, which formed the brief preamble to the Arsenic Act of that year, is nowadays almost daily illustrated by a succession of inquests and criminal trials, investigating suspected cases of poisoning due to the use of arsenical sheep-dip or weed-killer. After the sensational Greenwood case in 1920, the Pharmaceutical Society drew public attention to the possible advisability of altering the conditions under which these poisonous substances were supplied and used. More recently experts have declared that alternative non-poisonous preparations are available, and that the time has come to prohibit altogether the use of arsenic for agricultural and horticultural purposes, rather than to continue the present dangers of benevolent toleration. A recent article in the *Solicitors Journal* criticises the defects and anomalies of the existing law. The restrictions imposed by the Arsenic Act of 1851 were valuable. They insisted on the colouring of arsenic before sale; they forbade sale to persons unknown or under age; and they required the particulars of each sale to be entered in a book, and to be signed by the salesman, and (if he could write), the purchaser. The Act did not apply to arsenic in prescriptions by a legally qualified medical practitioner, or—whatever distinction the words may import—"a member of the medical profession." The Pharmacy Act of 1868 introduced a general control of the sale of arsenic and other scheduled poisons (the list of which has been extended

from time to time), by restricting to registered chemists the power to sell, by prohibiting sales to persons unknown or not vouched for, and by requiring entries of sales to be made in a Poisons Book. No doubt it was deemed right that a dangerous poison should be sold only by a qualified chemist, who would use his skill and judgment in warning the purchaser of the nature and quality of the drug supplied. In 1908, however, came the important relaxation which has enabled ironmongers, storekeepers, and other unqualified persons all over the country to sell arsenic freely. Section 2 of the Poisons and Pharmacy Act of 1908 declared that the restrictions of the 1868 Act were not to apply to poisonous substances containing arsenic, tobacco, or tobacco alkaloids sold for agricultural and horticultural purposes, provided that the seller was duly licensed by the local authority and that he observed the prescribed regulations. The obtaining of a licence seems to be a mere formality; the renewal of a licence is an easier process still. Regulations of 1909 require that sheep-dip and weed-killer must be kept in a separate drawer or closed receptacle, apart from other goods, and must not be sold at the same counter as food for human consumption. Regulations of 1920 (replacing earlier requirements) add that the poisonous substance must not be sold except in enclosed vessels or receptacles as received from the manufacturers, secured from leakage and labelled with the name and purpose of the substance, the word "Poison," and the seller's name and address. These rules are excellent so far as they go; but the law places no restriction on the storage or possession of arsenic in this form, nor is there any prohibition on sale to persons under age. Thus, as our legal contemporary observes, a chemist may not sell half an ounce of powdered arsenic to a youth under age who wants it for killing rats; but a corn-dealer may sell a gallon of liquid arsenic, or a pound of powdered arsenic made up into a packet and called "weed-killer," to any boy of 16 whom he knows, and who says he wants it for killing weeds in his father's garden. Further, it appears that even unlicensed persons are often found offering weed-killer for sale, either in ignorance of the law, or in the mistaken belief that any tradesman may sell these goods if they are supplied in the original package sent out by the manufacturer. The time seems ripe for reconsidering whether arsenical preparations are so indispensable in the garden, or on the farm, as to justify the exception made in their favour in 1908, and also whether the conditions of their supply and use are not, in any case, too free from control. It may be said that the public is weary of incessant restrictions, and that a would-be murderer will always manage, somehow, to equip himself for his nefarious purpose. The present laxness of the law, however, is in marked contrast with the retraints imposed by statutes in 1920 upon the possession of firearms and of dangerous drugs. It would be instructive to have statistics of the proportion of poisoning cases in which the obtaining of arsenic in the form of sheep-dip or weed-killer has "facilitated the commission of the crime."

THE BROAD TAPEWORM IN NORTH AMERICA.

THE past year has added considerably to what is known of the distribution and hygienic significance of the plerocercoid of *Diphyllobothrium latum* in the region of the great lakes of North America.[1] This stage is by no means restricted to the Michigan Peninsula. Infected fish have been reported by T. Vergeer[2] from Lakes Winnipeg, Manitoba, Nipigon, and Winnipegosis, from Lac la Biche, and from the Lesser Slave Lake; while H. E. Essex[3] has proved that *Cyclops brevispinosus*, *C. prasinus*, and *Diaptomus oregonensis* act locally as first larval hosts. It must be emphasised, however, that man is not the only definitive host of this cestode. There is, for example, a moderate infection of fish in the smaller Canadian lakes far from towns. In these parts, when Indians or white men while fishing for trout catch wall-eyes and great northern pike—fish constantly infected with the plerocercoids—such unwanted fish are fed raw to dogs, of which every man seems to have at least one, and some a pack; and the dogs are readily infected, as many as 19 parasites having been found in one animal.[4] Moreover, the broad tapeworm has been reported from the fox, *Vulpes fulvus*, and from the domestic cat. The grey wolf, lynx, mink, marten, racoon, and otter feed on fish, and Vergeer has readily infected the cinnamon bear, which in the spawning season has been known to scoop as many as 20 fish out of the water on to the bank before starting his meal. Man is thus but one of a number of definitive hosts used by *D. latum*, and that he cannot be the main one is shown by Vergeer's calculation[5] that the United States imports yearly from Canada upwards of 6,000,000 plerocercoids hidden in fish, while only about 200 cases of human infection have ever been reported from the United States. The risk to man can hardly be considered great enough to justify that ruining of an important industry, with great loss to concerns dependent on it, which would follow the exclusion of Canadian fish from the United States. Careful disposal of human sewage is evidently insufficient to prevent infection of fish, but man is readily and fully protected by the cooking of his fish food, and woman will lose her preponderant tendency to infection when the Jewess gives up her habit of tasting raw fish to test her skill in flavouring it.

[1] See THE LANCET, 1928, ii., 337.
[2] Canad. Med. Assoc. Jour., 1928, xix., 692.
[3] Jour. Parasitol., 1927, xiv., 106.

PECTOSE AND ITS ALLIES.

THE class of substances, known as the pectins or pectic compounds, which occur in apples, pears, and other fruits as well as in such roots as turnips and carrots, form a valuable stand-by for the jam maker, and this circumstance has brought them within the purview of the Food Investigation Board. Mrs. M. H. Branfoot (née Carré), the author of a study[6] made on behalf of the Board, has herself contributed greatly to the clarifying of our knowledge of these obscure substances to which over 300 workers have directed their attention during the last 100 years. The essential difficulty of studying the pectins is that they are uncrystallisable, they form no well-defined compounds, they are difficult to purify, and chemically they seem to lead nowhere; and this in spite of the fact that such skilled workers as Regnault, Cross and Bevan, Winogradsky, and other well-known botanists and chemists have sought to clear up their relations. Braconnot seems to have been the first to realise (in 1825) that these bodies existed, but Frémy first described (in 1840) the parent substance, pectose, as an alcohol- and water-insoluble body associated with cellulose in the cell-walls of plants, but chemically very unlike cellulose. Later workers found pectose difficult to isolate in an unchanged state; acids and alkalis may dissolve it with production of pectin and pectic acid, but they also change it. Pectose, indeed, appears from the work of Fellenberg and Carré to be formed by the union of cellulose with pectin; acid hydrolysis resolves it again into its constituents. Ehrlich concluded that the natural pectin of plants may be conceived as a complex anhydro-arabinose-galactose-methoxy-tetra-galacturonic acid. The replacement of a variable number of methoxy-groups by cellulose may be supposed to confer insolubility on the complex, which would be hydrolysable to varying degrees by acids and alkalis, or by other hydrolysing agents such as the natural enzymes found in plants. Having regard to the difficulty of ensuring that one is dealing with a chemical individual, it is not surprising that such

[4] Jour. Amer. Med. Assoc., 1929, xcii., 607.
[5] Jour. Infect. Dis., 1929, xliv., 1.
[6] A Critical and Historical Study of the Pectic Substances of Plants. H.M. Stationery Office. Pp. 154. 3s. 6d.

different empirical formulæ as $C_{28}H_{42}O_{24}$ and $C_{64}H_{48}O_{64}$ should be attributed to pectins from different sources. Mrs. Branfoot, after fully discussing the matter, concludes that pectin is a neutral methoxy-ester of pectic acid, represented by the formula $C_{39}H_{58}O_{33}$, and yielding 11·76 per cent. of methyl alcohol, whilst the basal molecule of fully de-methoxylated pectic acid is $C_{35}H_{50}O_{33}$, with a characteristic calcium content of 7·66 per cent. Intermediate tri-, di-, and mono-methoxy forms appear to exist, the jellying power, according to A. G. Norman, diminishing with the number of methoxy groups. Laboratory methods for the extraction and determination of pectic compounds from fruits and other vegetable products are described in this study, as well as commercial methods useful for the maker of jams and fruit jellies who wishes to stiffen his products, and so to avoid the troubles of the housewife whose jam will not set. The use of these products is specially called for when fruits deficient in pectose, like apricots, pineapple, and strawberries, are concerned. This practice is vigorously defended by the author who has made a particular study of the apple, following the changes of pectose into pectic acid, cellulose and methyl alcohol via pectin and the pectinic acids during ripening and the disappearance of these substances during rotting. The changes are made visible by staining sections with ruthenium red and other appropriate dyes. The monograph should appeal to the plant physiologist as well as to the fruit preserver and to the flax retter whose interest in pectic substances is confined to getting rid of them.

THERAPEUTICS FOR STUDENTS OF PHARMACY.

THE large number of words derived from the Greek *pharmakon* must be a puzzle to the lay mind; some refer to the doctor and his art, others to the pharmacist and his craft. But the line of pharmacy for the chemist, and pharmacology and therapeutics for the doctor, is one overstepped on both sides, and one which must be overstepped in training, at any rate, if a sound and liberal education is to be given. The strife which sometimes arises between doctor and chemist is not over what each learns, but what each practises. The professor of pharmacology and chemistry in the University of Washington has deliberately decided to write for the student pharmacist a text-book[1] on pharmaceutical therapeutics, including in his sub-title "with pharmacology." The book is eminently readable, running smoothly to the English ear; its general arrangement is therapeutic, according to the bodily system for which the drugs are most frequently applied. In his preface Prof. Lynn sets out a reasoned and, it seems to us, a reasonable defence of his action. There are, he tells us, a number of modern and very satisfactory books on pharmacology and toxicology for the medical student and practitioner, but no one has attempted to present, for the pharmacist, such a field in simple manner with general but without a practical therapeutic application. It is this gap in general therapeutic teaching which the writer wishes to fill, for the teaching of pharmacy is otherwise difficult. In describing each drug he considers the physiological actions most important in the treatment of disease and most significant in the diagnosis and treatment of poisoning. The principles of its therapeutic employment, which are closely associated with these actions, are given in outline without any attempt to describe the practical application. Therapeutic information is supplied for students of pharmacy and for their education rather than for their practice.

The danger of imparting general information to those who are not meant to apply it cannot have been overlooked by Prof. Lynn. The temptation to prescribe for such common ills as headache, constipation, and general debility is seldom resisted by the pharmaceutical chemist when pressed by a customer dissatisfied with his medical attendant or reluctant to pay a fee. If the pharmaceutical chemist is more interested in the purpose than in the technique of his profession he will study therapeutics with zeal and may find irksome the limitation of his life-work to the dispensing of remedies prescribed by others. It must be remembered, however, that the status and responsibilities of the chemist vary in different lands and in different epochs—for example, in France his profession stands exceptionally high. In Great Britain, too, there are signs of the expansion of opportunities in pharmaceutical chemistry, since the laboratories of the Pharmaceutical Society of Great Britain and Ireland have, in recent years, taken on important new duties. It is, however, mainly in one direction of therapeutics that the modern student of pharmacy is enlarging his experience; the many biological remedies now on the market are being standardised year by year according to methods which require special training, and an entirely different outlook will be demanded in future years if the increase in the number and popularity of these remedies is sustained. The curriculum of the student of pharmacy is likely to become almost as crowded as that of the student of medicine. Whether there is room for therapeutics, even in its most general sense, remains doubtful.

[1] Pharmaceutical Therapeutics with Pharmacology, Posology, and Toxicology. By Eldin V. Lynn, Ph.D., Professor of Pharmacology and Chemistry, University of Washington, College of Pharmacy, Seattle. London: McGraw-Hill Publishing Co., Ltd. 1929. Pp. 431. 20s.

ENOUGH BUREAUCRACY AND NOT TOO MUCH.

A SPEAKER who last week addressed the Law Society's meeting at Bournemouth on the Rise of Bureaucracy chose as one of his supreme examples the departmental order which requires a cowman to wash his hands before milking. Bureaucracy is undoubtedly a grave disease of the body politic. Lord Hewart has forsaken his judicial detachment to attack it as the "new despotism"; Lord Wolmer has been exposing the defects of a nationalised post-office; the medical profession knows its own troubles in the departmental aspects of health insurance and in the Statutory Rules and Orders about the supply of dangerous drugs; many members of the public have their favourite instances of petty restrictions tolerable only in war-time, and of official tactlessness and stupidity. But are there many champions of the ancient liberties of England who are anxious to go to the stake on behalf of the right to supply dirty milk? The direct legislation of Parliament specifically enacted that Milk and Dairies Orders should—amongst other things—prescribe the precautions to be taken for protecting milk against infection or contamination and for preventing danger to health from the sale of infected, contaminated, or dirty milk. Accordingly, the Order of 1926 directs that any person engaging in the milking of cows or the distribution of milk shall keep his clothing and person in a cleanly condition, and that all cowkeepers shall see that the hands of the milker are thoroughly washed and dried before milking—with other precautions for the same purpose. It is true that this adds to the list of crimes which sufficed Elizabethan England, and that prosecutions for dirty hands may encourage lawyers to take nice points as to the exact meaning of "thoroughly washed." But if the country wants clean milk Parliament must require the observance of elementary precautions, and the Ministry of Agriculture must frame certain minimum standards. Parliament might, of course, legislate about such details itself instead of delegating its authority to a department; but Parliament is one of the worst possible bodies for legislative purposes; it is too big and too busy to attend to details. As for the loss of personal freedom which the Bournemouth speaker's instance involves, there are copious parallels in other fields of public health. Where an individual's act or neglect can imperil the health and safety of others he may have to surrender something of his

freedom. The notification of infectious disease, quarantine, vaccination, the cleansing of verminous persons, and the detention of the insane—all these have elements of interference and compulsion which are familiar in our Public Health Acts and in the even more stringent variants of local legislation. If, in a matter like milk-supply, the choice lies between the Bournemouth speaker's remedy of laissez-faire and the Ministry of Agriculture's Order, the public may swallow a small dose of bureaucracy with no ill-results.

CONCERTED STUDY OF TUBERCULOUS INFECTION.

MANY of those who write in praise of team-work in research have never tried it; the research mind can only rarely be harnessed in a team. There are quick workers and slow, intuitive thinkers and plodders who add one to one with painstaking care, men whose gifts lie in manipulative skill, and those to whom technical laboratory work is an abhorrence. No doubt each individual can find work suitable to his needs, given the opportunities, but thrice blessed is he who can bring them together into an efficient and harmonious team. Such is seen in the record of a decade of work by a team of American investigators, organised by the Kenneth Dows Research Fund of Johns Hopkins University and Hospital, and published in a limited edition regardless of cost.[1] Each research is an entity in itself, but each bears upon the rest; all the papers have appeared from time to time in the *American Review of Tuberculosis* and an interval of seven years separates the first from the last. Throughout these studies the workers have had the advantage of the use of a culture of human tubercle bacilli isolated by Trudeau at Saranac in 1891. At the time of isolation it exhibited what might be called standard virulence for guinea-pigs, but after two or three years of incubator existence it underwent a noticeable diminution of virulence. This diminution proved, as time went on, not to be progressive to a vanishing-point, and the strain has retained a certain degree of infecting power for guinea-pigs, which has not changed during the last 20 years. Its newly acquired, though lessened, infectiveness has become a fixed and static property resisting all ordinary methods that have been aimed at changing it. The studies were designed primarily to elucidate two main problems in tuberculosis immunity—viz., the part played by the lymphatics in the localisation of tuberculous disease, especially in its chronic pulmonary form, and the mechanism by which this localisation favoured the development of the immunity processes. Early in the story comes Dr. W. S. Miller's study on the normal histological distribution of the lymphatics of the human lung, followed by his wax reconstruction models of a single tubercle in the lung, which enable the observer to visualise in three dimensions what he has hitherto only looked at on a plane surface. These models are probably unique. Then follow researches on the vascular supply and lymphatics of the lung of the guinea-pig and the rabbit by Dr. Miller, Dr. Krause, and Dr. H. S. Willis. Each research emphasises minute points of difference between these two animals which to the uninitiated might appear to be of no practical value whatever; but in subsequent papers the picture of lymphatic mechanism is built up to show that these differences are not devoid of meaning. Dr. Krause makes it clear that, although the tracheo-bronchial lymph nodes of the rabbit are small and unimportant, the intrapulmonary lymph tissue is large in amount and is supplied by blood from the pulmonary artery; consequently when intravenous infection with tubercle bacilli takes place, an intra-pulmonary fixation of the bacilli by these lymph nodules follows. Here the anatomical distribution of the lymph nodules determines the focalisation of the disease. For the same reason the presence of large tracheo-bronchial glands in the guinea-pig determines the early localisation, in this case not in the lungs but in the hila. From this point Dr. Krause goes on to show how foreign particles passing through the lungs may be "embolised." If they are arrested there, they may remain in situ or they may be conveyed into tissue spaces and thence to the intra-pulmonary lymphoid tissue as in the rabbit, or the hilum nodes as in the guinea-pig. Again, therefore, it is seen that the lymphatics are the determining points of focalisation. But not only do they focus infection, they control the rate of the dissemination of tubercle bacilli from the portal of entry onwards. In the normal guinea-pig dissemination takes place within three hours; in the immune pig, after subcutaneous reinfection with a virulent strain of bacilli, a great delay occurs in the transmission of tubercle bacilli from the point of entry to the customary places of localisation within the body takes place. The outstanding feature is not complete inhibition but retardation. This work on the lymphatics of these two animals, which are so frequently used in laboratory experimentation, is a valuable contribution to the pathology of tuberculosis. The importance of the lymphatics in the spread of this disease through the body has been recognised by all pathologists since the days of Sylvius, but the fact that variations in the lymphatic distribution in different animals might be responsible for so much variation in the pathological picture has hitherto not been clearly recognised. Its bearing upon the morbid anatomy of human tuberculosis is obvious. Finally, the work of Dr. Krause and Dr. Dorothy Peters suggests the existence of two factors in this mechanism—namely, tissue allergy and immunity. The allergic reaction is called into play by the tissue contact of immune animals with dissociated tuberculo-protein or with tubercle bacilli, and this is followed by an accelerated development of the characteristic nodular tubercle.

[1] Studies on Tuberculous Infection. By Allen K. Krause, William Snow Miller, and Henry Stuart Miller Kenneth Dows Tuberculosis Research Fund, Johns Hopkins University, Baltimore.

THE HEALTH OF SEAMEN.

THE Seamen's National Insurance Society is an organisation bound by its constitution to accept every seaman who applies for membership without regard to his age, state of his health, or any outside consideration. The membership is not of a specially selected class, and for this reason some figures set out at the annual meeting held in June last and now published in the report of progress for 1928 are of interest. Throughout the eight years ended in December, 1928, on the average 12 per cent. of their members received sickness benefit, but in both 1927 and 1928 the number represented 15 per cent. Detailed examination of the records does not indicate any exceptional causes for this increase in sickness. In 1927 influenza had a marked effect, but in 1928 the number of influenza cases was below the average. A more encouraging feature is the low incidence of tuberculosis and venereal disease. The membership of the Society as certified by the Ministry of Health has averaged a little under 60,000 during a period of 16 years, and the cases of tuberculosis have averaged little over 100 a year during this period. During the last eight years the deaths from tuberculosis have averaged one-seventh of 1 per cent. per annum. In the same period the known incidence of venereal disease has also been small. The Society's doctors have treated rather less than 150 cases a year, this number including members who have received medical benefit after being eligible for sickness benefit. The cases of venereal disease, as far as can be ascertained, represent one-fourth of 1 per cent. of the members of the Society. Sir Norman Hill, the chairman, in announcing these figures said that he believed them to present a very different picture from that drawn from other sources, but he knew of no grounds upon which their accuracy could be questioned. As regards tuberculosis there could be no possible reason for

underestimate. Indeed, the Society was entitled to get substantial help from the local authorities in every proved case. He made no claim that the figures shown by the Society's records are generally applicable to all seamen, and put them forward only to suggest that those figures derived from other sources require closer investigation than appears to have been given them. Among the difficulties of assessing the sickness of seamen is, of course, the impossibility of obtaining reliable estimates of the total number of seamen. An individual may be described as a seaman on very slender grounds, especially in death certificates. The title is often used by those who find only seasonal employment at sea, and may be retained long after the man has left the sea to follow a permanent occupation on the shore.

A TREATMENT FOR EMPYEMA IN INFANCY.

EMPYEMA is still a very dangerous condition in infancy. In the United States, Spence [1] in 1920 found in a total of 204 cases that the mortality was 64 per cent. in the first year and 50 per cent. in the second. Cameron and Osman's [2] figures in this country three years later are in close agreement with Spence's, showing 66 per cent. mortality in the first year and 50 per cent. in the second. Of many methods advocated as means of reducing this high death-rate, one which has found favour on the continent is the use of optochin, a preparation of ethyl-hydrocupreine hydrochloride which has been shown to have an inhibiting effect on pneumococci in vitro. Woringer,[3] of Strasbourg, employs it as follows. As much pus as possible is aspirated from the chest, and a 5 per cent. solution of optochin is then injected into the pleural cavity in a dosage of 25 mg. per kg. of body-weight, the total dose not exceeding 500 mg. (10 c.cm.). This procedure is repeated three or four times at intervals of one to two days, and it is stated that the general condition of the child usually improves and the fever diminishes. If not, a second course of injections may be given and even a third or fourth. Some authorities, after aspirating the pus, wash out the pleural cavity with 100–200 c.cm. of a 0·5 per cent. solution, but Woringer is opposed to this on the grounds that it may cause shock and death. He has treated 36 children by his own method and 24 of them recovered completely. Five were operated on secondarily and successfully—and in the light of later experience he thinks unnecessarily—and there were six deaths. The mortality in the first year of life was 29 per cent. (7 cases) and in the second year 36 per cent. (11 cases). Eighteen children over the age of two were treated without a death. Optochin is said not to have any effect on the staphylococcus or streptococcus, and its action is purely local. After the first injections pneumococci are still present in the pus and stain by Gram's method, but it is stated that they will not grow in culture. Fever sometimes recurs as a result of pocketing and if this happens each pocket must be injected separately or the pneumococci, deeply embodied in fibrous deposits, may soon recover their virulence. Hence in Woringer's opinion no case should be pronounced cured until fever has been absent for several weeks. The pus disappears usually in two or three weeks, and radiography shows that even big masses of fibrinous deposit may be entirely resolved within five or six months. But since optochin has been found dangerous when injected intravenously in pneumonia it may well be asked whether there is any risk in introducing it in the pleural cavity. To this question Woringer replies that he has never seen any bad effects from its employment in the dosage recommended, and he even suggests that in some resistant cases the concentration should be cautiously increased from 25 to 50 mg. per kg. It is, of course, difficult to say how far any benefit from the treatment recommended is attributable to the repeated aspiration of pus. Woringer himself does not hold that the use of optochin will supersede operative measures, but he thinks it may be very useful, especially perhaps when it is desirable to defer operation owing to the coexistence of pneumonia and empyema.

[1] Spence, J. L.: Amer. Jour. Dis. Child., 1920, xx., 545.
[2] Cameron, H. C., and Osman, A. A.: THE LANCET, 1923, i., 1097.
[3] Woringer, Pierre: Rev. Franç. de Péd., Feb., 1929

EPIDEMIOLOGY IN ICELAND.

ACCORDING to a correspondent who has lately visited Iceland, and whose paper is concluded on p. 801 of this issue, "There are many striking differences in the behaviour of diseases in Iceland and other countries. A study of these differences might well throw important light on the ætiology of these diseases." As examples it may be noted that tuberculosis, which is declining in most civilised countries, is increasing in Iceland at rather an alarming rate. Poliomyelitis, on the other hand, according to the data supplied, seems to be clinically milder than when it is epidemic in similar environments such as rural Sweden—in spite of the fact that the high morbidity for such a small country suggests that the virus is spreading in an unsalted population. Islands have often been a fruitful field for biological research, as is well brought out by Russel Wallace in his classic "Island Life," because an insular environment permits the segregation, preservation, and evolution of fresh varieties of organisms, including man and microbe. In epidemiological research isolation is a tremendous asset, if not an essential requirement, since the factors involved are so numerous and complex that in areas where continual intermigration is going on between the hosts and parasites of neighbouring areas, the problems become almost hopeless of solution. This shows the importance of another noteworthy remark in our correspondent's article. "In such an isolated and sparsely populated country," he says, "an invading germ can be followed almost visually, as it passes from one lone homestead to another." From this it appears that Iceland is an ideal hunting ground for the epidemiologist. Of recent years, however, it has become more and more clear that epidemiological research, if it is to produce any useful results, must be prolonged over many years, and include extensive studies of the healthy as well as the afflicted, during inter-epidemic, as well as epidemic, periods. Ideally, at any rate, such research requires a team of medical ecologists which include among them clinicians, statisticians, bacteriologists, and (last but not least) a general biologist. Governments rarely care to subsidise such expensive and lengthy academic studies, which are unlikely to produce a visible or immediate return for their money. But should some great scientific organisation, such as the Rockefeller Foundation, be looking for promising material for epidemiological research, it almost seems as if Iceland, with its highly educated population, its learned medical men, and its natural geographical advantages, is the most promising field left in the world. The time is now or never; for as transport and intermigration become more rapid, frequent, and extensive every year, it will not be long before Iceland loses its unique character as a potential key to the mechanism of epidemics.

REGULATION OF THE DIABETIC DIET.

NOWADAYS a large proportion of patients take an interest in their own complaints and try to understand them as far as they can. Dissatisfied with the diagnosis of "an internal inflammation," they wish to know if their ulcers are gastric or duodenal and are often able to argue at length about the relative merits of medicinal treatment and a short-circuit. When this attitude leads to self-prescribing and treatment, pitfalls inevitably open before patient and doctor, but so long as it only means intelligent coöperation it may be valuable to both of them. Diabetes is perhaps the outstanding example in which

such coöperation is important, and several manuals and sets of tables have been published for the use of patient and practitioner alike. The latest contribution is a "Diet Summary in Average Servings for Diabetics,"[1] by Dr. P. J. Cammidge. The basis, as the title implies, is a standard diet made up of helpings of food as they appear at the table. From this the diet for any particular patient is determined by a process of trial and error controlled by the usual examinations of blood and urine. The main articles of diet are grouped under the headings of protein, carbohydrate, fatty and miscellaneous foods. Average helpings are given in ounces and the relative amounts of protein, carbohydrate, and fat are set out in grammes and also in "rations." The "ration" is an arbitrary unit which has been found to facilitate working: 20·0 g. of protein = one protein ration (P.R.), 5·0 g. of fat = one fat ration (F.R.), and 4·0 g. of carbohydrate = one carbohydrate ration (C.R.). Thus the average serving of boiled cod is 3½ oz. containing 20·0 g. of protein and 0·2 g. of fat, and forms one protein ration. The tables offer a ready means of varying a diet within the limits laid down. A patient taking, say, six carbohydrate rations at a meal may have it in any one of the following forms, each one of which is regarded as an average helping: ¾ oz. sago, 1 oz. wheat flour or macaroni, 2 oz. chestnuts, 4 oz. potato, 5 oz. broad beans, or one average sized pear (5½ oz.), banana (7½ oz.), or apple (7½ oz.).

While this summary is apparently written in the first place for the use of medical men, it is one which could be handed with advantage to any intelligent patient if his diet had first been stabilised and if any experiments or alterations were made under supervision. The tables have been carefully compiled; they are practical and simple, and they should prove of real help in relieving the monotony of the ordinary diabetic diet. In the necessarily condensed introduction are several controversial statements. It will not be generally accepted that actual appeal to the balance is rarely required after a little practice. This may be, and often is, true in cases on diet only, but in insulin cases, particularly if large doses are required, a check should be made at least once a week even if daily weighing is not necessary to prevent errors creeping in. Discussion is also invited by the statement that if the patient is able to utilise less than 40 to 50 g. of carbohydrate daily, insulin will probably be required. Future editions would be made more useful by the addition of a general index of foods, arranged alphabetically for quick reference to the various groups. These criticisms apart, the brochure may be warmly recommended.

ASPIRATION DURING TONSILLECTOMY.

PULMONARY abscess is a very rare sequel of tonsillectomy but it is greatly dreaded, the more so because it follows a comparatively trivial operation. At one time it was taken for granted that inflammation in the lung was due to the anæsthetic, but its occurrence when local anæsthesia is used shows at any rate that this is not always so. As we pointed out a fortnight ago (Sept. 28th, p. 673) two theories at present hold the field: first, that the complication is a result of inhalation of infected material during the operation; the second, that it is caused by the lodgment in the pulmonary vessels of emboli from the site of operation. In this connexion it may be noted that pulmonary abscess is not uncommon after other operations, notably laparotomy. Our annotation described some experiments designed to test the inhalation theory, and it may be of interest to draw attention now to some other observations whose object was the same. Attempts have often been made to ascertain, by bronchoscopy and by indirect laryngoscopy, what is the quantity of material aspirated and what is its dispersion through the tracheobronchial tree during tonsillectomy under inhalation anæsthesia. Impressed by the inadequacy of these methods, R. V. May, T. W. Thoburn, and H. C. Rosenberger, of Cleveland,[1] have made an elaborate radiographic investigation of 25 patients, aged from 3 to 12 years, during and after the operation of dissecting out the tonsils under a general anæsthetic. The radiopaque material employed was iodised oil and olive oil in equal parts, of which 2 to 3 c.cm. was dropped slowly on to the posterior pharyngeal wall and immediately removed by swabbing. Radiograms of the anæsthetised patient were taken before and after the instillation of the oil, after the dissection of each tonsil, after removal of the adenoids, and six hours after operation. Secretions were removed on gauze sponges, except in two cases where a suction-pump was employed; these both showed aspiration into the bronchial tree. Of the results, 48 per cent., or almost half the cases, showed evidence of aspiration; in all but four cases the iodised oil had been eliminated by the time that the fifth radiogram was taken, after removal of the adenoids, and only one case showed any remaining after six hours. The authors justly claim that the use of skiagraphy in investigating the degree of aspiration during operation is much more informative than the methods previously employed. They conclude that aspiration may be diminished by the adoption of the extreme Trendelenburg position, by constant and thorough removal of all pharyngeal secretions, by a technique producing a minimum of mucous secretion and hæmorrhage, and by a degree of anæsthesia which preserves the irritability of the laryngeal and tracheal reflexes; further, that some degree of aspiration is unavoidable in all operations requiring an inhalation anæsthetic. The investigation does not, of course, decide the question whether pulmonary abscess is caused more often by embolism or by inhalation.

A POST-GRADUATE course for old students of the London Hospital will be held next week from Wednesday (Oct. 16th) until Saturday, and a provisional programme appears in our Medical Diary. Communications may be addressed to Mr. Hugh Cairns at the hospital.

THE Bradshaw lecture of the Royal College of Surgeons of England will be delivered at the College at 5 P.M. on Thursday, Nov. 14th, by Mr. R. P. Rowlands, and the subject will be a Review of the Surgery of the Gall-bladder and Bile-ducts. Students and others who are not Fellows or Members of the College may gain admission by presenting their visiting cards.

As we have already announced, the Harveian Oration of the Royal College of Physicians of London will be delivered at the College by Sir Wilmot Herringham on Friday next, Oct. 18th. Dr. J. A. Arkwright, F.R.S., will give the Bradshaw Lecture on Nov. 5th, his subject being the Virulence of the Micro-organism in Infective Disease. Dr. G. F. Still's FitzPatrick Lectures, on the History of Pædiatrics in the Seventeenth and Eighteenth Centuries, will follow on Nov. 7th and 12th; and the Lloyd Roberts Lecture will be given on Nov. 14th by the Rt. Hon. H. A. L. Fisher, F.R.S., whose subject is An Oxford Movement. The Harveian Oration will be at 4 P.M., and all the lectures at 5 P.M.

[1] A Diet Summary in Average Servings for Diabetics and others suffering from Disorders of Metabolism. By P. J. Cammidge, M.D. Lond. London: Baillière, Tindall and Cox. 1929. Pp. 8. 1s. (6s. per doz.).

[1] Jour. Amer. Med. Assoc., 1929, xciii., 589.

DONATIONS AND BEQUESTS.—Among other bequests the late Mr. J. D. Kay left £1000 to the Manchester Royal Infirmary.—Mrs. Polly Wharton, of Brights Cottage, Heckmondwike, left £1000 to the Heckmondwike Urban District Council upon trust to apply the income in defraying the expenses of sending to the seaside poor and sick children resident in the district, and £500 to the Heckmondwike Nursing Association.

The Clinical Interpretation of Aids to Diagnosis.

A Series of Special Articles contributed by Invitation.

XLVII.

THE MICROSCOPIC EXAMINATION OF FÆCES.

PART II.*—BACTERIA.

THE conditions of warmth, moisture, and pabulum obtaining in the intestinal tract are almost ideal for promoting the growth of micro-organisms, and a great variety of bacteria is to be found in the fæces. They are, however, really outside the body itself, and are to be regarded as essentially saprophytes, although under certain circumstances almost any of them may enter the body and become pathogenic. There are four great groups of bacteria normally appearing in the fæces; the coliform bacilli, the streptococci, the anaerobes, and the acidophile bacilli. The streptococci and acidophiles retain Gram's stain, as do most of the anaerobes, while the coliform bacilli are decolorised by Gram's method. A generation ago Combe advocated the simple staining of a smear of the fæces by Gram's method, and drew inferences from the proportion of bacteria which retained the violet coloration, to those which were decolorised and took up a counter-stain. Although this procedure has not led to results of practical application, a variation in the proportion of the bacteria of the four groups named does nevertheless occur, and one of the chief factors influencing this variation is the diet taken by the patient.

Influence of Diet.

The intestinal tract, which is sterile at birth, is soon found to contain bacteria. Normally about one-third of the dried fæces of healthy people on a mixed diet consists of bacteria. During the period of milk-feeding, the acidophile group predominates largely; but with the onset of mixed feeding, the bacterial distribution changes and soon resembles that of the adult, the coliform bacilli becoming the prominent group. The coliform and anaerobic bacilli preponderate with a high protein diet; whilst the *B. acidophilus* is increased on a high carbohydrate diet. Increase of streptococci follows an addition of glucose or cane sugar to the diet, and the numbers of viable streptococci are greater after a saline purge. Elimination of many putrefactive anaerobic bacilli and other proteolytic organisms, and reduction of the coliform bacilli, can be brought about by a lacto-vegetarian diet, with plenty of fruit and green vegetables, especially if lactose be added. Cultures of *B. acidophilus* may be given in milk to hasten the change of flora.

In addition to the normal inhabitants of the bowel, certain pathogenic organisms occur in disease, such as typhoid, dysentery, and tubercle bacilli. These will be dealt with before discussing the conditions under which the normal bacteria may cause disease.

The Typhoid-Paratyphoid Group.

In the typhoid-paratyphoid group of diseases the bacteria may appear in the stools from the first week onwards, and are recovered in one-third to one-half of the cases. Though other methods of diagnosis are more reliable—such as blood cultures during the first ten days, and the Widal reaction after that—culture of the stools is useful as a control. Bacteriological technique has much improved as the result of the experiences of the war; it is now agreed that before a positive finding is reported, the suspected organisms must not only conform to requirements in motility and fermentation of sugars, but also must be agglutinable by a standard serum. *Typhoid* and *paratyphoid* B bacilli, though less common than formerly, occur still in mild epidemics; *paratyphoid* A, an Eastern type, was more often met with during the war, brought by the troops coming from India. These diseases must be notified. The bacilli continue to be excreted in gushes for some time during convalescence, so that several negative reports at intervals should be obtained before the patient returns to ordinary life. Sometimes it happens that a patient, though apparently well, continues to pass enteric bacilli at intervals; he becomes a "carrier," and a source of unwitting infection of the rest of the community. Such a person should be isolated under medical supervision, and should be debarred from any occupation which entails the handling or distribution of foodstuffs. Unfortunately, in these cases, it is often difficult to get rid of the infection, which may continue for a long time in such places as the gall-bladder.

Dysentery Bacilli.

In cases of colitis due to infection with dysentery bacilli, the organisms can be recovered from the mucopus in a large majority of the cases in the acute stages; in chronic cases they are rarely found. Indeed it may well be that bacillary dysentery is always an acute infection, though sometimes quite a mild one; and that a chronic colitis following an attack of dysentery is kept up by non-specific bacteria as a secondary infection. The laboratory report should differentiate between dysentery bacilli of the *Shiga-Kruse* and of the *Flexner-Y* types. The former infection is a serious affair, since the *Shiga* bacillus has a toxic effect on the nervous system as well as on the intestine. Nowadays a good antitoxic serum is available. Infection with *Flexner* dysentery bacilli is milder; it may be troublesome, however, and even fatal in infants, or in elderly or debilitated patients. There are at least five members of this *Flexner-Y-Hiss* and *Russell* type, and no standard serum is available. Eliminative treatment, for example by sodium sulphate, is the best.

A number of bacilli, not true dysentery, but capable of producing colitis, are grouped together as *para-dysentery* bacilli, of which perhaps the best known are *Morgan's No. 1* bacillus in the summer diarrhœa of children, the *Sonne* bacillus associated with dysenteric symptoms, and the *Bacillus enteritidis* of *Gaertner* and *B. aertrycke* in food poisoning. The allied *B. suipestifer* (hog cholera bacillus) is important for animals and probably sometimes for man. There are also others whose claim to be regarded as pathogenic is not yet accepted. These will be dealt with later.

Tubercle Bacilli.

A report of *tubercle* bacilli can only rarely be unexpected. Their presence in sufficient numbers to be detected in a routine examination will occur only when there is gross clinical evidence of chronic bowel trouble. In children with phthisis, in whom all sputum is swallowed so that none is available for direct examination, pus containing tubercle bacilli may be passed in the motions. In suspected cases of intestinal tuberculosis, special methods of concentration with antiformin and inoculation of a guinea-pig may be required.

Cocci.

Staphylococci are not inhabitants of the intestine. When their presence is reported, a local infection of the lower bowel by abscess or fistula-in-ano should be sought for; otherwise it is a negligible contamination from the skin. *Streptococci*, on the other hand, form one of the important groups of the normal intestinal flora, and there are several varieties which may at times be pathogenic. The usual differentiation made is by their action on blood cells, so that they may be classified according as they produce a green pigment, or completely hæmolyse the blood corpuscles, or have no effect upon them. All three classes may be present in fæces. The non-hæmolytic one (*enterococcus*) is the commonest. It is usually not pathogenic, though it is reputed to be so at times, as a secondary infection following ulcerative states of the bowel. A variety of

* Part I., on Cytology and Animal Parasites, appeared last week.

the enterococcus is believed by Bargen to be the causative organism in chronic ulcerative colitis; but this is not generally accepted by pathologists. The other two classes, green and hæmolytic streptococci, may also become pathogenic. If they invade the blood stream or tissues of the body, they may cause severe symptoms, but their presence in the fæces is not necessarily significant.

Other Micro-organisms.

The vibrio of *cholera* may be found in epidemics in the tropics, but does not occur in these islands. *B. pyocyaneus* (the bacillus of blue pus), *B. proteus* (a putrefactive bacillus often found in great numbers in watery offensive stools), *B. lactis aerogenes* (allied to *B. Friedlander*, the pneumobacillus), *B. fæcalis alkaligenes* and *B. pseudoasiaticus* are rather harmless findings in the fæces, though possibly they may become pathogenic at times in other situations.

The other groups of fæcal bacteria, anaerobic and acidophile, as well as the spirochætes and yeasts—except the ray fungus of actinomycosis—are not important so long as they remain in the lumen of the bowel; though it may be expected that as our knowledge of the biochemical products formed by these organisms from food-stuffs increases, there will be some evidence found on which to form conclusions about a possible "intestinal toxæmia."

While one-third of the dried weight of normal fæces consists of the bodies of dead bacteria, these bacteria in the lumen of the bowel are really, as already mentioned, outside the limits of the body proper, and are as unlikely to gain entrance to the body, unless there is a breach in the mucous membrane, as are skin organisms without some damage to the skin epithelium. Such a break in the mucous membrane of the bowel occurs in any abrasion or ulcer, and there is no doubt that a secondary infection of dysenteric and tuberculous ulcers takes place with the ordinary cocci and bacteria of the bowel. Even when the site of invasion is not obvious, we know that a septicæmia with colon bacilli may occur, and that these are often excreted by the kidney causing irritation and inflammation of the urinary tract. Just before death, too, the blood is often invaded by bowel organisms, which can be recovered in blood culture; being a terminal state only, this septicæmia of intestinal organisms is not important, as by the time it sets in the bowel wall has probably lost its normal protective power.

Criteria of Pathogenicity.

These conditions are, however, exceptional. What importance should be assigned to the bacteria which remain in the lumen of the bowel? It must be noted that the media used for culture of micro-organisms are artificial ones; though selective for some bacteria, they may even inhibit others. The amount of growth on culture media may bear little relation to the numbers of bacteria present in the fæces, or to their pathogenicity. Too much emphasis should not be laid on an apparent increase in numbers, such as an excess of streptococci; it has been shown above that great variations in numbers of streptococci occur with change of diet, and of the consistency of the stools. In pernicious anæmia and other conditions with subacidity of the gastric juice, there is a great numerical increase of the normal inhabitants of the bowel, *B. coli*, *streptococci* and especially the anaerobe *B. welchii*. But there is no evidence that these organisms differ qualitatively from those found in healthy persons, or that any individual type of organism is specifically related to pernicious anæmia. It is necessary, too, to avoid the fallacy of treating the patient for such conditions as the presence of coliform bacilli, which are atypical in having a delayed power of fermenting lactose. The usual *B. coli* rapidly produce acid and gas in lactose media, whilst most of the known *pathogenic* Gram-negative bacteria do not show this reaction with lactose in ordinary media. There is an intermediate group which ferments lactose after an interval of several days—some of them may even produce so much ammonia from peptone digestion that an acid reaction never appears—which are classed alternatively as *para-dysentery* or *para-colon* bacilli. A few of these are of known pathogenicity, a few of known harmlessness; there is little evidence that the majority of them exert a harmful action on the animal body. The quality of delayed fermentation of lactose is not therefore significant. A further group of these colon bacilli is found to grow in the presence of normal active serum; some even hæmolyse red blood corpuscles. These serum-resistant and hæmolytic *B. coli* may be pathogenic, but we have no certain evidence on this point. The same is true of hæmolytic streptococci. Their ability to live on blood, digesting and destroying the red corpuscles, makes them, at any rate, potential parasites, and, if they are found elsewhere in the alimentary tract—at the roots of teeth, in the crypts of tonsils, or in the discharge from nasal sinus infection, as well as in the fæces—their possible importance cannot be denied. But if the evidence we have of the pathogenicity of these groups of bacteria is doubtful, evidence of their relevance in a particular patient is usually unattainable; the presence of any sort of specific immune body in the patient cannot be demonstrated by serological tests.

Vaccines from Fæces.

The value in treatment of vaccines made from the fæces, though widely assumed in this country, is not proved by bacteriological criteria, and does not rest on the same scientific basis as, for example, typhoid preventive inoculation, or the treatment of diphtheria and tetanus with serum. Nor has it the support of solid clinical proof, such as that of the value of vaccination against small-pox. It rests mainly on clinical impressions, which, as time goes on, may need to be revised, or, at the least, defined and classified.

In view of the great difficulties which confront anyone attempting to assess the possible pathogenic significance of fæcal organisms, therefore, no clear indications can be found for their use in vaccine-therapy. Antibodies to them may be formed by a patient into whom they are injected, but we have no means of knowing whether these have any specific action or are likely to help the patient in resisting his disease. Although vaccines have a proved place in bringing about protection against subsequent infection, their rôle in treatment is by no means securely founded. Until further positive evidence is accumulated, therefore, we have no warrant for using any but those derived from organisms with known pathogenic action; the promiscuous use of vaccines from other fæcal organisms is unlikely to lead to useful results.

S. W. PATTERSON, M.D., D.Sc., M.R.C.P.,
Physician, Ruthin Castle.

HOSPITALS AND MOTOR ACCIDENTS.—The British Hospitals Association is asking the Government to introduce a measure making it obligatory upon motorists to insure against third party risks, and empowering hospitals to recover from the insurance companies the cost of treating motor accident patients.

PUBLIC ASSISTANCE COMMITTEES AND HOSPITALS.—Under Section 1 of the Local Government Act of 1929 the London County Council will, on April 1st, 1930, take over the functions of the Metropolitan Asylums Board, as well as of the Boards of Guardians within its area. That area has been divided into ten sections, under a Public Assistance Authority of 48 members, 16 of whom will be coöpted from outside the Council, assisted by local committees. Hospitals are to be dealt with by a Central Public Health Committee, which is the Council's old Public Health Committee reconstituted. The county will be divided into five hospital areas, each of which will be coterminous with the boundaries of a group of boroughs. The scheme of rearrangements adopted by the Middlesex County Council provides that the Public Assistance Committee shall be composed of members of the Council only, coöption being confined to the local committees. Among the hospitals to be taken over by Middlesex are the North Middlesex (900 beds), the Hounslow Institution (800), Park Royal (778), Edmonton House Institution (700), and the West Middlesex (325).

Special Articles.

OXIDATION-REDUCTION POTENTIAL.

A SUMMARY OF RECENT WORK.

BY N. F. MACLAGAN, B.Sc.

(From the Courtauld Institute of Biochemistry, Middlesex Hospital.)

IT has been known for many years that the animal body derives its energy from combustion—that is, oxidation—and the exact analysis of this process is therefore of fundamental importance in physiology. In dealing with any form of energy there are two factors to be considered, which are best illustrated in the case of heat energy. Everyone is familiar with the distinction between temperature, which may be termed the intensity factor, and the amount of heat, measured in calories, which is the capacity factor. The different nature of these two quantities is made clear by the experiment of dropping a red-hot needle into a bowl of hot water; the heat capacity of the needle is much less than that of the water, yet heat passes from the needle to the water. Chemical energy may be split into two factors in an exactly similar way, and in the special case of oxidation we may regard the oxidation-reduction potential as the intensity factor, exactly analogous to temperature, which is indeed frequently called heat potential. Oxidation-reduction potential therefore decides which one of two systems will oxidise the other, just as the temperature decides the direction in which heat will pass when two systems are connected; to complete the picture oxidising capacity as estimated by titration may be compared with the heat capacity (calories).

The conception is perhaps made clearer by taking the further example of neutralisation of a base by an acid, where the acidic power may be factored into titrable acidity (capacity) and hydrogen-ion concentration (intensity). This case is also of special interest on account of the similarity in the methods of measuring hydrogen-ion concentration and oxidation-reduction potential. In both cases the first approach was through the use of certain dyestuffs called indicators. Litmus is an acid base indicator which is red in acid and blue in alkaline solutions; moreover, it changes colour in a certain relatively narrow range of pH, so that in this range its colour is an index of the pH. Similarly, methylene-blue is blue in the oxidised and white in the reduced condition, and changes colour in a narrow range of oxidation-reduction potential; to revert to the first example, it may be compared to a thermometer which indicates heat potential over a limited range. Ehrlich [7] was the pioneer in this field, and he was able to demonstrate differences in the reducing power of various organs with respect to indophenol blue and alizarin blue. Much work of a similar character failed to produce any definite advance owing to the fact that the relationships between the different dyes were not understood; also no zero of oxidation-reduction potential had been established, so that quantitative deductions from the experiments were impossible.

In 1920 Gillespie [9] published the first observations upon the electrode potential of bacterial cultures, and it was this work which led W. M. Clark and his colleagues to their "Studies on Oxidation reduction," [4] which have thrown such a flood of light upon the whole problem. With the aid of electrode measurements they have been able to arrange a large number of dyes in an orderly series on a definite scale of oxidation-reduction potential, and as a result of their work it is now possible to make a fair estimate of the oxidation-reduction potential by observing the colour of a suitable dye. In order to understand the relation between the electrode and the dye methods, it is necessary to consider in more detail the chemistry of oxidation.

The Conception of Electron Transfer.

The older chemists regarded oxidation as an addition of oxygen or a subtraction of hydrogen, and reduction as the reverse. But with the development of the ionic theory this view has given place to a more general one, which may be conveniently illustrated in the oxidation of ferrous to ferric chloride

$$2FeCl_2 + Cl_2 = 2FeCl_3.$$

It is known that both $FeCl_2$ and $FeCl_3$ exist in solution mainly in the ionised form, so that this reaction may be written

$$(2Cl^- +)\ Fe^{++} + Cl \rightleftharpoons Fe^{+++} + Cl^- (+2Cl^-).$$

Evidently the essential part of this reaction is the transference of an electron—the unit negative charge of electricity—from the ferrous ion to the chlorine atom, which is thereby converted to an ion; so that the chlorine may be regarded as merely taking up the electron liberated in the oxidation of ferrous to ferric ion, which is therefore represented thus:

$$Fe^{++} \rightarrow Fe^{+++} + e.$$

This idea is of very wide application, and in general oxidation and reduction are associated with a loss and gain of electrons respectively

$$ox + e^- \rightleftharpoons red \qquad \text{(Equation I.)}.$$

On comparing this equation with that for the neutralisation of a base by an acid

$$H^+ + OH^- \rightleftharpoons H_2O$$

it is evident that the reducing intensity of a solution is determined by the "concentration of free electrons" in the same way that the acidic intensity is determined by concentration of hydrogen ions. Apparently also a plate of noble metal may be regarded as an "electron electrode" in the same sense that a film of adsorbed hydrogen is regarded as a hydrogen electrode. Thus, when an electrode of plain gold or platinum is immersed in a solution, the potential set up is a measure of the reducing intensity of the solution and is called the oxidation-reduction potential E_h.

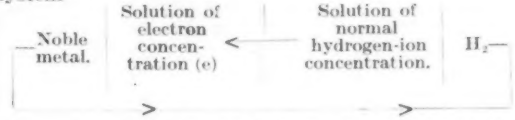
It should be noted that this treatment is purely formal, and that no objective reality is to be attached to such terms as "concentration of free electrons." There is, in fact, no evidence of the existence of free electrons in aqueous solution, and a difference in the mode of action of the hydrogen and oxidation-reduction electrodes is postulated which is probably fictitious; moreover, for the sake of simplicity, concentration is here substituted throughout for activity. The equations obtained by more rigid methods are, however, identical with those derived on the above hypothesis which has the advantage of presenting a clearer mental picture of the terms involved.

The oxidation-reduction potential is a single electrode potential whose absolute value cannot be determined, since a second single electrode must be coupled with the first before a measurement can be made. It is the practice to refer all such measurements to the normal hydrogen electrode, to which a potential of zero is arbitrarily assigned—that is, when an oxidation-reduction electrode is coupled with a normal hydrogen electrode the potential developed is attributed entirely to the former. This convention is expressed in the following equation:

$$E_h = -\frac{RT}{NF} \log (e) \text{ volts} \qquad \text{(Equation II.)}$$

when R = gas constant; T = absolute temperature; N = number of electrons transferred; F = the faraday.

This equation represents the potential difference of the system



the potential at the liquid junction being neglected. It is further agreed that E_h be taken as positive when

the current tends to flow as in the diagram. E_h is then an index of tendency to oxidise. Solutions having a positive E_h will oxidise, those having a negative E_h will reduce the normal hydrogen electrode. Also any solution will tend to oxidise one having a smaller, and tend to reduce one having a greater E_h than itself.

Reversible Reactions.

It is important to recognise that this treatment applies only to a perfectly reversible process, and herein lies the difficulty of applying it to living systems, whose processes are not in general reversible. However, we must consider together with this restriction the probability that many biological oxidations which are apparently irreversible proceed by a number of stages, some of which are truly reversible.

A further limitation of the theory outlined above arises when the reaction velocity is considered. The oxidation-reduction potential certainly decides in which direction the reversible reaction will proceed but does not say at what rate; this rate may be infinitesimally small, in which case the reaction does not proceed at all. The rate is, of course, frequently greatly affected by the oxidative catalysts, whose influence must therefore always be an essential factor in the problem.

The physical meaning of equation II. is revealed by application of the law of mass action of equation I.

$$(e) = K \frac{(red^-)}{(ox)}$$

Substituting in II.

$$E_h = \frac{RT}{F} \log K - \frac{RT}{F} \log \frac{(red^-)}{(ox)}$$

$$= E_o - \frac{RT}{F} \log \frac{(red^-)}{(ox)} \text{ (Peter's equation).}$$

E_o is a constant for any one reaction and is obviously equal to E_h when $(red^-) = (ox)$—i.e., at half oxidation.

It will have been noticed that the reductant in the above equations is an anion. This is a special case, but it is obvious that one or both of the reactants must exist in the ionised condition when an electron transfer is regarded as the essential process—e.g.,

$$ox + e \rightleftharpoons red^-$$

$$ox^+ + e \rightleftharpoons red$$

$$ox^+ + 2e \rightleftharpoons red^-$$

Thus the hydrogen-ion concentration may also affect the system as shown by the following equation:

$$H^+ + red^- \rightleftharpoons Hred.$$

In such a case it is usually only possible to measure the total reductant

$$S_r = Hred + red^-$$

and the relation of this to the active reductant red^- evidently depends upon pH. The following equation applies:

$$E_h = E'_o - \frac{RT}{F} \log \frac{Sr}{So} \quad \text{(Equation III.)}$$

where E'_o is a function of the pH.

It is interesting to note that this relationship between E_h and pH is a mutual one, so that changes in the oxidation-reduction system will affect the pH; the two equilibria are closely interconnected.

Equation III. is the basis of the indicator method of estimating oxidation-reduction potentials, which has been so thoroughly worked out by Clark and his colleagues. They have constructed E_h–pH percentage oxidation curves for a large number of indicators whose reduced and oxidised forms are differently coloured. If one of these dyes be added to a solution of known pH, in an amount so small as not appreciably to affect the existing equilibrium, the colour becomes an index of the oxidation-reduction potential. By choosing suitable indicators which change colour in the E_h (and pH) range under investigation a fair accuracy is obtainable.

Biological Applications.

The oxidation-reduction equilibrium is at least as important in the body as the acid-base equilibrium. It may therefore appear at first sight somewhat remarkable that the quantitative measurement of oxidising intensity—E_h—should have lagged so far behind that of acidic intensity—pH—in biology, but this is only the result of pushing the analogy too far. Neutralisation is evidently a unique process in aqueous solutions as it is a single reversible reaction in which the water takes part:—

$$H^+ + OH^- \rightleftharpoons H_2O.$$

On the other hand, the terms oxidation and reduction include a vast number of reactions, many of them irreversible, whose only common property is an interchange of electrons, and is thus not specifically related to the solvent. In addition, the interpretation of measurements is made difficult by our ignorance of the exact chemical mechanism of the simplest biological oxidation. The probable participation of reversible processes in these apparently irreversible oxidations has already been mentioned, but it would appear that few such processes have yet been found which are susceptible to electrode measurement.

It has been mentioned above that the earlier researches with indicators commenced by Ehrlich in 1885 did not produce any very definite results: the review of Needham and Needham[11] contains an excellent account of these researches. Clark and his collaborators have now removed many of the practical and theoretical difficulties, with the result that since 1920 there has been published much important work of which only the outstanding features can here be noticed.

The Reduction Potential of Bacteria.

The reduction potential of bacteria was first studied electrometrically by Gillespie,[9] who showed that anaerobic cultures developed increasingly negative potentials, the actual values obtained being very different in the few cases investigated. This was confirmed by Cohen, Cannan, and Clark,[4] who obtained similar results with cell suspension and who have also made some very interesting preliminary observations on the influence of glutathione on the development of these potentials. They conclude that the aerobic tissue cell or bacterial culture is roughly poised between +0·1 and 0·2 volts E_h. The system is not, however, in equilibrium with the atmospheric oxygen, which serves merely to oxidise the reducing substances elaborated in the cells at such a rate that the E_h is maintained within these limits. Under anaerobic conditions this controlling factor is removed and the E_h gradually falls, producing death of the cells (except in anaerobic organisms).

Evidently the classification of bacteria into aerobes and anaerobes has some reference to E_h. Quastel and Stephenson[12] concluded from their work on *B. sporogenes* that the behaviour of obligatory anaerobes is best explained on the assumption that they cannot grow above a certain potential. Similar results were obtained by Fildes,[8] who showed that the germination of spores of *B. tetani* failed to occur in media whose E_h was greater than +0·01 volts. Moreover, he explains the fact that this strain will not grow when injected into the guinea-pig by the incompatible E_h of the subcutaneous tissue fluid.

Intracellular Measurements.—In addition to these extracellular investigations, direct measurements of the intracellular E_h have been made by a method first introduced by Needham and Needham[11] which consists of making micro injections of suitable indicators into the living cell. This method has also been used by Brooks[1] Cohen, Chambers, and Reznikoff[5]

Rapkine and Würmser[13] Chambers, Pollack, and Cohen[3] and in view of the difficult technique it is perhaps not surprising that absolute agreement has not yet been reached. The aerobic potentials are mostly of the same order as those recorded by Cohen, Cannan, and Clark for bacteria and cell suspensions, but while the Needhams maintained that the E_h of the *amœba proteus* was unaffected by anaerobiosis, the later workers found a fall of potential under these conditions. It has been emphasised by Cohen, Chambers, and Reznikoff that three factors are concerned in the interpretation of the results of these experiments—the intensity, capacity, and rate factors,—and it is no doubt the difficulty of allowing for the last two which is responsible for the existing uncertainty.

In this connexion, Cannan's work on *mercuralis perennis* is of great interest[2]; this plant contains a pigment, hermidin, which is in fact a reversible oxidation-reduction indicator, so that the E_h can be found in this case under perfectly normal conditions. It proved to be about —0·1 volts.

Oxidative Enzymes.

It was shown by Dixon and Quastel[6] that the system consisting of a mixture of reduced and oxidised glutathione was an anomalous one, for the potential proved to be independent of the concentration of the oxidised form. This implies that the change from reduced to oxidised glutathione is an irreversible one and therefore cannot be studied in this way, but the production of a stable potential is still of great interest, especially as it is not certain that glutathione acts through the change from reduced to oxidised forms. The cystine-cysteine system is in the same class, and the researches of Michaelis[10] and co-workers on the electrode potential of cysteine is yielding valuable information about its metallic complexes. Compounds of this type have been shown by Warburg[14] to be intimately concerned with tissue oxidation, and while the mechanism responsible for these potentials is still uncertain it is considered probable by Michaelis and Flexner[10] that the sulphydril group is the principal poising agent in the cells.

In conclusion, it may be emphasised that accurate work on oxidation-reduction potential in biology has only been going on for about nine years, and that much of the time has been taken up with essential chemical preliminaries. The importance of the subject cannot be doubted, and it is reasonable to expect considerable advances in the near future.

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SALE OF ST. BARTHOLOMEW'S HOSPITAL LANDS.—The Charity Commissioners have sanctioned the sale of 346 acres of building land at Stanmore belonging to St. Bartholomew's Hospital. The price paid for 249 acres of Kenton Lodge Farm, Stanmore, is £62,736. An option, exercisable within 12 months, has been given on the purchase, for £24,137, of a further 95 acres adjoining.

ST. MARY'S HOSPITAL POST-GRADUATE COURSE.

THE post-graduate course held at St. Mary's Hospital during the first week-end of the winter session has become deservedly popular among practitioners. The attendance this year was as large as usual, in spite of the fact that other teaching hospitals are adopting the excellent plan of providing at this season of the year a short concentrated course. We publish on p. 751 of this issue one of the lectures delivered at St. Mary's, and abstracts of two of the other lectures are given below. We hope in the future to give further space to addresses delivered at St. Mary's and at other hospitals in London during this month. Mr. T. G. Stevens chose for his subject

Retention of Urine in Women.

Retention of urine, he said, though not a common trouble in women, might be a serious one if imperfectly treated. Its causes ranged from hysteria to a retroverted gravid uterus. Retention of urine might complicate or follow labour, and might also follow operations, especially those for prolapse. It might also be the result of the pressure of tumours and other lesions. Hysteria in young girls might lead to retention of urine, from simple functional failure of micturition. Before making the diagnosis, hæmatocolpos, of which retention may be the first symptom, must be excluded, and also rare pelvic tumours. Hysterical stigmata should be looked for. All ordinary efforts to promote micturition should be tried before a catheter is passed, but this operation should not be postponed longer than 24 hours at the utmost. Usually all simple methods fail, and one passage of the catheter may cure. No doubt the discomfort of the passage has some effect, but suggestion plays a greater part. According to Mr. Stevens, retroverted gravid uterus is the commonest cause of retention of urine in women, but is frequently overlooked. The history is misleading, some women stating that they are "always passing water," when they mean that they are always wet from the dribbling overflow of a fully distended bladder. A fatal mistake is to treat such a case as one of frequency of micturition without a careful examination. *Any* micturition trouble in the presence of a large abdominal tumour ought to raise the suspicion of a distended bladder, and demands the passage of a catheter. The danger of retention with overflow is that of infection of the distended and atonic bladder. In such a bladder the results of infection are far worse than in common cystitis with an empty bladder. Sloughing of the mucous membrane may occur, and infection may travel up the periureteral lymphatics to the kidneys, with the production of multiple abscesses (surgical kidney), septicæmia, and uræmia. In common cystitis with an empty bladder ascending infection seldom occurs. In the absence of overflow the passage of a catheter prevents all these dire results, and once the bladder is empty a retroverted gravid uterus can easily be felt filling the pelvis. If this can be replaced easily with the fingers, as it often can, the cure is at once complete. If, however, manipulation fails, a cure can still be obtained by keeping the patient in bed, lying in the semiprone position, and by passing a catheter to empty the bladder every eight hours. If this method is adopted the uterus usually replaces itself in about three days. A large ring pessary in the vagina often assists the replacement, but will have no effect if the patient is walking about. It is never necessary to induce abortion to cure these cases, but spontaneous abortion sometimes occurs, especially if efforts at finger replacement are too vigorous. Mr. Stevens pointed out that while retention during labour may be caused by the pressure of the fœtal head on the neck of the bladder, after labour inability to micturate is solely the result of fatigue and the stretching of the abdominal muscles. The patient is

unable to make even the small straining effort necessary for micturition in women; it is interesting to note that few women realise that any effort at all is involved. After prolapse operations retention may also be due to the fact that the slightest strain causes pain in the new perineum, from stretching of sutured tissues; hence the patient at once inhibits the effort and micturition may fail. If with the first strain the act starts, the patient usually has no further trouble. Drugs, such as hexamine or boric acid, which irritate the bladder, will sometimes assist the act, but usually in post-operative cases a catheter has to be passed very gently every eight hours for several days. The only common tumours which compress or stretch the urethra and neck of the bladder are cervical fibroids, but occasionally fibroids in the body of the uterus may have the same effect, especially if the uterus is retroverted. It is rather a stretching of the urethra than actual compression which leads to retention in these cases, in which the catheter always has to be passed a long distance, sometimes as much as five inches, before the urine will flow. Mistakes may arise if the catheter is not passed sufficiently far, for no urine will be obtained, and the distended bladder may be taken for an ovarian cyst. Ovarian tumours rarely cause retention, but when they do it is because they are incarcerated in the pelvis. Incarceration may be brought about by adhesions in Douglas's pouch; but certain ovarian tumours have the broad ligament stretched over them, and thus tend to lever up the uterus out of the pelvis and to press it against the neck of the bladder and pubes. A pelvic hæmatocele, if large enough, may also press the uterus against the neck of the bladder, and so may widespread pelvic suppuration. Once any pelvic mass has caused retention an abdominal operation for its removal is imperative, the bladder being kept empty by catheter until the operation can be done.

Diabetes.

Dr. C. M. Wilson said that sepsis was like a magnifying mirror that stood between the observer and the diabetic, and until it was removed it was impossible to obtain an undistorted view of the diabetic's condition. He brought forward examples of recovery of carbohydrate tolerance following removal of sepsis. A woman who required 50 units of insulin daily was able to achieve the same results with 8 units a few weeks later after the removal of septic tonsils and septic teeth. A musician, whose unstable temperament made treatment by both dieting and by insulin equally unsatisfactory, had 10 per cent. sugar in his urine. After drainage of a septic bladder he became sugar free, without any change in the rest of the treatment. Dr. Wilson pointed out that the removal of tonsils since the introduction of insulin was a reasonably safe procedure if an adequate amount of carbohydrate was given and utilised, that the consumption of fat in the days previous to the operation was drastically curtailed, and that the minimum of anæsthetic was given. He was, however, far from advocating that surgical procedure should be lightly embarked upon. The evidence of sepsis must be adequate. When this was absent, or had been removed, it was necessary to decide whether the treatment should be confined to dieting, or whether insulin should be administered. Earlier he had been reluctant on grounds of expediency to use insulin except in those patients where its use could not be avoided, but at the present time he was using it in a much larger proportion of cases. The general condition of the patient was often much more satisfactory with insulin, and its use enabled him to cut down the amount of fat that was necessary. He aimed at giving a diet to an adult containing 80 to 100 g. carbohydrate, 1 g. of protein for each kg. of the patient's weight, and sufficient fat to maintain the weight rather below normal without acidosis. The limitation of protein was frequently neglected, since it was overlooked that sugar could be formed from protein, and that the proportion of protein given was an important factor in the production of acidosis.

Dr. Wilson then dealt with the development of premature arterio-sclerosis in the diabetic; coma, which had been the chief cause of diabetic deaths before the introduction of insulin, was being replaced in that rôle by arterio-sclerosis. It therefore became important to inquire why the diabetic was specially prone to arterio-sclerosis. He thought there was some evidence that the excessive fat in the diet of the diabetic was an important factor, by predisposing to excess of cholesterol in the blood. If that were true it was necessary to keep the fat in the diet within limits, and in doing this insulin was most helpful by keeping the carbohydrate element high, with a corresponding fall in the amount of fat. The diseased heart muscle of many middle-aged and elderly diabetics seemed to demand a higher level of sugar in the blood than normal, if it was to be properly nourished; a practical application of this demand was to be found in the caution required in any attempt to lower a high blood-sugar in a diabetic with diseased heart muscle by insulin. It was easy to provoke an attack of angina pectoris by the administration of insulin, and if insulin were used with patients liable to such attacks it was necessary to use a high carbohydrate diet. Dr. Wilson had been impressed with the importance of equal caution in the use of insulin in diabetics with retinitis. He then discussed diabetes in children, and particularly in children whose glucose tolerance curves were not typically diabetic, and yet were not normal. Such cases should be watched; he had seen two such children develop typical diabetic curves.

He felt that the education of the diabetic patient, upon which ultimate success largely depended, did not receive sufficient attention. The diabetic should learn his diet and the value of each element in it. It was possible to simplify this to a great extent for him. He should learn, too, how to test his urine for sugar, and how to avoid coma and gangrene. Many diabetic patients were seen in the out-patient department without inspection being made of their feet. Coma was largely a preventable accident. Nobody would think of driving a car without an insurance against third party risks; it was far more important for the diabetic to master the technique of insulin administration. He might not need it for the present, but the day would probably come when an infection would render it necessary, and his knowledge gained at leisure might then save his life. Exercise was very helpful; it was the tissues and not the kidneys that removed the excess of sugar from the blood, yet it was a common practice in hospitals to see diabetic patients confined to bed for weeks without any provision for exercise. The attempts made in recent years to persuade the practitioner that diabetes was a simple affair were very well in their way, but we had to realise that in few medical diseases could the doctor be of as much assistance to his patients as in diabetes, and that if he was to render this assistance he must himself master the broad principles on which the diabetic diet of to-day rests, and the details which make it practicable to transfer that knowledge to the patient.

CHILDREN'S HOSPITAL, BELGRADE.—Through the Save the Children Fund (28, Gordon-street, London, W.C. 1) an appeal is being made for this hospital by the members of the British Legion who have just returned from the annual congress of the Inter-Allied Federation of Ex-Service Men at Belgrade. They call to remembrance Dr. Katherine Macphail's work in creating a modern, well-equipped hospital of 50 beds and an out-patient department through which more than 100,000 children have passed during the last ten years. The infant mortality in Serbia is "appallingly high"—one in three. The hospital trains Serbian girls as nurses under the supervision of a British matron. It is partly maintained by the Jugo-Slavian Government, but a further £2000 has to be found, two-thirds of which has to be collected by Dr. Macphail. This is the only hospital exclusively for children in the country.

SCOTLAND.

(FROM OUR OWN CORRESPONDENT.)

Association of Insurance Committees.

AT the annual meeting in Ayr of the Scottish Association of Insurance Committees Provost Irvine, of Coatbridge, the President, commented on the need for specialist and consultant services, not only as an advance towards a complete and satisfactory medical service for the insured population, but also as a sound financial proposition, saving its cost by reducing the amount paid out in sickness benefits, and ultimately enabling approved societies to make substantial contributions or even to meet the whole expenditure upon these services. He also criticised the hiatus now existing between the statutory age for leaving school and the statutory age for entering into national insurance. From the period of infancy till the age of leaving school health services were continuously available, at considerable cost it is true, but with satisfactory results. Yet, for those between the ages of 14 and 16 years, no provision for health service was made. This serious anomaly stood self-condemned. Provost Irvine is a well-known pioneer in Scottish public health work, and understands both sides of the question.

Drugs for Insured Persons.

One of the best parts of the Scottish system of National Health Insurance is the central checking bureau at Glasgow, through which all prescriptions pass, and are there subjected to technical criticism and pricing. It was stated at the Ayr meeting that the number of prescription forms handled last year on behalf of the 54 insurance committees in Scotland—namely, 2,655,737—was a decrease of 93,000 on 1927, and 104,000 less than the record year of 1926. The value of the prescription forms, exclusive of the cost of insulin, was £147,328, a decrease of £4410 on 1927. The average price per form at 13·31*d.* was very slightly above the average for the previous year, 13·24*d.* The tariff price of 100 units of insulin has been reduced by successive stages from £1 6*s.* 8*d.* to 2*s.* 7*d.*, and it was rumoured at the meeting that a German firm had offered to supply London hospitals for a year with insulin at 1*s.* for 100 units. The bureau has now handled 32¼ million prescription forms at a total cost of 1¾ million pounds. The vexed questions of who should foot the bill for drugs for insured persons while in hospital led to the passing, by a large majority, of the following motion: "That the cost of drugs, including insulin, supplied to insured persons under treatment in voluntary institutions should be a charge against the drug fund of the insurance committee, instead of having to be met from the funds of the voluntary institution." The original Insurance Commission and the later Board of Health never saw their way to accept this proposition; it remains to be seen whether the insurance committees will be more successful with the new health department.

Working Out the 1929 Act.

Mr. John Jeffrey, Secretary of the Department of Health, gave the meeting his views on the effect that the Local Government (Scotland) Act, 1929, will have on the work of insurance committees. Endless complications would, he said, ensue unless steps were taken to achieve harmony in the relationship between the general practitioner and the specialist in hospital and dispensary services. When a patient was referred to a hospital or dispensary the very fullest medical history sheet should accompany him, and just as surely when he returned to the care of his insurance practitioner the fullest information regarding his condition and treatment should be supplied by the specialist in whose charge he had been. Mr. Jeffrey said he had been advised that 20 to 25 per cent. of insured persons receiving treatment from their panel doctors were in need of specialist advice. The health insurance funds had failed to meet that requirement, but under the hospital organisation of the 1929 Act it should be possible to bring to the aid of the insured person all the requirements of equipment and specialist services, while retaining the traditions of unfettered work. He went on to speak of the advantage to the general health of the community if some system could be devised whereby each insurance committee should supply to the local authority statistical information on the nature and extent of sickness among insured persons in the area. At present the local authority had no knowledge of the prevalence of ordinary sickness, or of the nature and causes of that sickness, or whether any action on its part could prevent or reduce such sickness. Now that the insurance committee and the public health authority were to coöperate the gap could be filled up.

Dr. Kinloch envisaged the development of a local authority hospital service with everything in the nature of elaborate equipment and specialist skill available for the insured population through their panel practitioners. This provision would in time release insurance committees from most of their present commitments on additional benefits, and enable them to plan a comprehensive extension of the insurance medical service embracing the dependents of insured persons not covered by the local authority service.

A Crematorium for Edinburgh.

Over 20 years ago a movement was started to provide a crematorium for Edinburgh, and a company formed in July, 1928, under the chairmanship of Lord Salvesen, lately acquired from the corporation two and a half acres of the Easter Warriston Estate, at a cost of £3000, on condition that dividends paid on the share capital should not at any time exceed 6 per cent. per annum. The late Sir Robert Lorimer was the architect, and the original mansion house has been adapted partly to form the crematorium and partly to form a chapel. The whole cost of buildings, roads, grounds, and furnishings is expected to be about £10,000. Hitherto all Scottish cremation has been done in the Glasgow Crematorium.

A New Hospital for Cripple Children.

On Oct. 1st the Duchess of York laid the foundation-stone of the new Edinburgh Hospital for Cripple Children. Sir David Wallace, chairman of the committee, said that sufficient money had been raised to justify the commencement of the building. The site extended to 14 acres, and its large size would permit of the children being educated in the open air. Some would be trained in workshops so arranged that the patients could work in the open air and the sunlight. It was proposed, said Sir David, that major and minor clinics should be formed throughout the various counties under the scheme, and at the earliest possible time children treated in the hospital would be sent to those clinics, after which the necessary treatment could be carried on in their homes under careful supervision, and in close relation with the central staff of the hospital. I understand that of the sum of £70,000 aimed at, some £55,000 has already been raised.

IRELAND.

(FROM OUR OWN CORRESPONDENT.)

Dispensary Salaries in Co. Mayo.

FOR many years the salaries of poor-law medical officers in County Mayo have been markedly lower than those of any other county in the Irish Free State. Not only were the salaries inadequate, but they were very uneven, so that medical officers in certain districts were drawing only half the pay of their neighbours doing approximately equal work. Many appeals had been made to the county board of health to establish an equable scale of salaries for the whole county, but the appeals were fruitless. Attempts by the Department of Local Government

and Public Health to persuade the Board of Health to move were equally useless. At length, however, the Minister has found it necessary himself to intervene, and by sealed order he has fixed the salaries of the several medical officers in the county. The new salaries are based on a scale of £200 a year, rising by annual increments of £5 a year to a maximum of £300. Each medical officer gets credit for all his pensionable service under the board. The immediate increase of salary to the several medical officers varies from nil to £160 a year, and averages £57 a year. The number of dispensary medical officers in the county is 30, and the immediate increase in salaries amounts to £1706 10*s*. This is the first occasion on which a whole scale of salaries has been established by sealed order over the heads of the local authority, and it is important for medical officers elsewhere that the precedent has been established.

Antivaccination and its Costs.

County Wexford has been the one county in Ireland in which the antivaccinationist movement gained any foothold, and for some years past its inhabitants have been very inadequately vaccinated. Within the past year or two, however, the Department of Local Government and Public Health determined to enforce the laws concerning vaccination, and legal measures were taken to compel the local authorities to fulfil their statutory duties. Reluctantly enough they are instituting prosecutions of those who neglect to bring their children for vaccination, and they find that each prosecution costs them nearly £1. There are said to be some 18,000 defaulters in the county, so that the total cost may prove to be considerable. At its last meeting the Board of Health made the naïve request to the Minister for Local Government and Public Health to give them a grant from public funds to enable them to enforce the laws. Having neglected its duty for years, the board finds the expense of fulfilling its accumulated obligations too heavy, and it suggests that the general taxpayer should come to its aid.

MEDICINE AND THE LAW.

The Law of Murder: Confession Without Corpse.

IT was not till 1926 that (as one result of the Coroners (Amendment) Act) it was possible to hold an inquest in the absence of a dead body. The possibility or impossibility of prosecuting a charge of murder without the proved existence of a corpse was discussed afresh last month. A man walked into a London police station and gave himself up as a self-confessed murderer. He said that one night in August last he met a woman named Rose while he was under the influence of drink, quarrelled with her, and flung her over the parapet of Waterloo Bridge, at an exact spot which he described. When he was charged before Sir Chartres Biron, the police informed the court that no body had been found, no woman named Rose was missing, and the man had not been seen in company with any woman that night, but had been seen alone in a public-house. They added that to throw a body over the bridge meant lifting the body up some seven feet, and required great strength, and that no screams were heard, either by a constable on duty 50 yards off or by a night-watchman slightly farther away. The magistrate, not wholly convinced by the confession, dismissed the charge. This course leaves the police free to prosecute afresh if new evidence becomes available. A confession, undoubtedly, can be adequate evidence, provided that it is clear and unequivocal. So said the Court of Criminal Appeal 20 years ago, in a case where a mother confessed that she had burnt her baby's body. But the police, who receive many strange confessions when any criminal mystery becomes a public sensation, are aware that abnormal mental states may prompt such statements, and they examine them with a care which sometimes becomes scepticism.

English criminal procedure is reluctant to see an accused person self-convicted. This tradition or instinct militates against the acceptance of a well-known police magistrate's recent suggestion that an accused person should be not only a competent but also a compellable witness. And English judges know the dangers of finding murder charges to be established when no dead body has been discovered. Coke, in his Institutes, gives a quaint anecdote of a case where the murderee returned after the supposed murderer had been hanged. An orphan girl was brought up by her uncle, and, one day, when he was correcting her for some fault in the method usual at the time, she was heard to cry out "Oh! good uncle, kill me not." Next day she was not to be found, and as the uncle stood to inherit property at her death, he was put into jail on suspicion of murder. Released on bail to give him a chance to produce his niece, he stupidly produced another girl of the same size, dressed in his niece's clothes. The trick was discovered, and he was hanged for murder, but anon the niece appeared, proved her identity, and successfully claimed her estate. She had run away into the next county instead of going to school the morning after her uncle beat her, and she had been kindly entertained by strangers who took pity on her. Coke tells his tale to point the double moral that judges must not be too hasty in assumptions in murder trials, and that innocent persons must not play silly tricks as the uncle did. A famous case of the same kind, reported in the State Trials, is that of the Perrys. Two brothers and their mother were found guilty of murder and hanged, and in a few years' time the supposed victim reappeared. There is a dictum of Sir Matthew Hale that he would never convict of murder unless either a dead body is found or the fact of the murder is proved. The latter alternative occurs in murders at sea, where the body is thrown overboard. The leading case is *R. v.* Hindmarsh (1792), where a seaman murdered his captain. No body could be produced, but there was sufficient evidence of the accused's declared intention, and of the actual struggle in which the captain was seen to be pitched into the sea.

A Dangerous Rat Poison.

The death of an Alton farmer from cyanide poisoning, as a result of blowing a rat poison powder down a rat hole in a closed shed by means of a bellows, has been noted in several daily papers. It is not quite clear what was the exact nature of the powder in question, although its name "cyanogas" would suggest to anyone acquainted with drugs or elementary chemistry that it was highly poisonous. A man may, however, be a good farmer without much knowledge of the Pharmacopœia, and such a man has a right to expect that poisons should not be put in his hands without full instruction for use. The coroner in this case described the directions as, in his opinion, carelessly drawn. The technical adviser of the manufacturers said it was dangerous to use the powder with a bellows or, indeed, in an unventilated shed; he considered that the instructions were strict in regard to ventilation. It is, no doubt, very difficult for a technologist to realise the extraordinary risks which people unused to handling dangerous materials will take. For this reason such rat poisons as barium carbonate, squill mixtures, and the like should suffice the general public, and the use of more deadly preparations be confined to professed vermin killers. The use of cyanides was prohibited in the city of Paris by an edict of the police last year, and they should only be supplied with the most explicit instructions for their use. Poisonous gases are more easily evolved than controlled or dissipated, and it is dangerous to disperse poisonous powders by blowing.

A HOSPITAL BURNED DOWN.—Aberdare and District General Hospital was totally burned on Sept. 27th, when two firemen lost their lives and a third was seriously injured. There were over 80 patients in the wards but they were all safely removed, at great risk to the matron and nurses. The damage is estimated at £20,000.

Correspondence.

"Audi alteram partem."

MALIGNANT TUMOURS IN FOWLS.

To the Editor of THE LANCET.

SIR,—The explanation offered in your last issue (p. 697) by Dr. A. M. Begg and Dr. W. Cramer for the appearance of Rous sarcomata in fowls which they had injected with extracts of fowl pancreas and mouse carcinoma—namely, that sufficient traces of the Rous agent were retained in a mortar after the latter had been washed in running water—may satisfy them, but it does not apply to the experiment of ours which they cite. Our material was merely minced with sterile scissors in a sterile Petri dish, and was not ground in a mortar, nor had any Rous material been in use at or about the time. Further, the bird that developed the tumour was one in a series of 23 inoculated with the same tissue, and none of the series came in contact with fowls bearing Rous tumours.

Perhaps I may be allowed to add that our tumour was at first histologically distinguishable from the ordinary Rous sarcoma, that one at least of Dr. Murphy's tumours produced by testicular extract was quite distinct, and that the tumour produced by Dr. Maisin through the action of ionium nitrate on grafted embryo tissue was again different.

I am, Sir, yours faithfully,

ARCHIBALD LEITCH.

Cancer Hospital Research Institute, London, S.W., Oct. 7th, 1929.

INTERPRETATION OF THE WASSERMANN REACTION.

To the Editor of THE LANCET.

SIR,—As one who has long contributed to your columns on the subject of the interpretation of the Wassermann reaction, I venture to lay before your readers a few criticisms of Dr. T. E. Osmond's article on this subject appearing in your issue of Sept. 28th (p. 677). I begin by quoting three sentences from an admirable leading article in THE LANCET of March 2nd (p. 453):

1. "Even when the test is made in laboratories where routine procedures are most carefully standardised under the direct personal supervision of an expert, the reaction given by a patient not actually undergoing treatment may vary in an unaccountable manner . . ."
2. "Two years ago a series of comparative tests were performed by pathologists working in different laboratories, all of whom used substantially the same technique. The results differed by as much as 25 per cent."
3. "It is true that the exact relation of the degree of strength of the Wassermann positive readings to the severity of infection is unknown."

In the same issue of THE LANCET appeared an article by myself in which I said:—

"During the last 20 years I have reiterated my opinion that while the Wassermann reaction was a good servant it was a bad master, that the test was clearly not specific, that there appeared no logical reasons why other similar chronic infections should not produce a like reaction, and that, therefore, no one should be dogmatically branded as a syphilitic on the evidence of a positive Wassermann reaction unsupported by any other historical, clinical, or pathological evidence."

The League of Nations has recently published the Report of the 1928 Copenhagen Conference on the "Sero-diagnosis of Syphilis." This conference was attended by pathologists of 16 nations, and the resolutions which they passed seem to suggest that Dr. Osmond's dogmatic assertion in the first sentence of his article is not corroborated by world opinion. Dr. Osmond says:—

"Provided that a satisfactory technique is employed and the test carried out by a competent pathologist a positive Wassermann reaction (++ or +) means that the patient is infected with syphilis—recent or remote. The only exception to this rule is 'yaws.'"

It is true that this initial dogma is a little hedged against in some later sentences, such as "no case should be labelled syphilis on the strength of a single isolated positive Wassermann," "the fluctuating Wassermann—on one occasion positive and another negative—is now recognised by most workers." and in his concluding summary "a positive result nearly always means syphilis, if there is a doubt it should be repeated and confirmed." In view, however, of his initial dogma carefully placed so as to catch the eye of those who will not read the whole article, I cannot but feel that the subsequent less dogmatic remarks were made, not because Dr. Osmond doubted the truth of the dogma contained in his opening sentence, but because he had read the Copenhagen Report.

This report contains eight resolutions passed by the conference, from which I will make quotations from four; they are:—

1. "The Conference is of the opinion that the best of them (flocculation tests) may be regarded as equal in value to the best of those which depend on fixation of complement (Bordet Wassermann)."
2. "The Conference recommends that in order to secure the most reliable information to the clinician, at least two different sero-diagnostic methods should be used."
3. "The Conference recommends that the serologist should check the accuracy of his tests by regular and very frequent reference to clinical data."
5. "The Conference wishes to reiterate with particular emphasis: (3) that except in the case of a few well-defined pathological conditions, syphilis is indicated with a degree of probability, which closely approaches certainty, when several tests performed according to different methods give a positive result."

These resolutions contain opinions widely differing from, and in my opinion much more in accordance with facts than, that expressed in the opening sentence of Dr. Osmond's article which I have quoted, and which I believe to be incorrect and misleading.

I am, Sir, yours faithfully,

Harley-street, W., Oct. 2nd, 1929. H. WANSEY BAYLY.

CURES AND PREVENTION.

To the Editor of THE LANCET.

SIR,—I cannot allow the address of Sir Farquhar Buzzard to the students of the University of Birmingham to pass without the strongest protest. It is a frank confession of the failure of the accepted methods of treatment of disease that is mainly of lesions produced by microbes in the human body, and it is this incapacity of medicine to produce efficient intravital germicides that has led to this confession of failure of Sir Farquhar Buzzard and the public criticism of our profession which he acknowledges to be just. For there is only one efficient intravital germicide in the Pharmacopœia, and that is anti-diphtheritic serum.

Is it not true that all our efforts in the teaching of the practice of medicine are concentrated on enabling the student to discover the tissues diseased, and to relieve the symptoms produced and most vitally to give that disease a name, with which the patient will be satisfied? We do not teach the student how to kill the microbes causing that disease and thus "cure" the disease. That is what our patients demand, and quite properly demand, and if we, as physicians, cannot do it, they will turn to those who say they can, as patients suffering from orthopædic troubles have turned to the unqualified, because qualified surgery was reputed not to be able to accomplish the very properly demanded cure. An accurately scientific method of preventing and aborting common cold is available, and we are in a position to say now that no catarrhal infection need ever become chronic. Anterior poliomyelitis can be so treated in the acute phases that the patient can be restored with little

or no damage to his musculature. The causative microbes can always be found.

I am sure Sir Farquhar will think that such a disease as disseminated sclerosis is an absolutely incurable condition. I can assure him that it is not so, that the cause can always be found, the infection of the spinal cord arrested, and the patient restored to his normal avocations. And so with practically all other microbial diseases that are now considered incurable. I expect these assertions of mine to be received with the usual derision, but I warn authoritative members of my profession that the writing is on the wall, and that they had better turn to the study of the production of "cures" if they wish us to survive as a profession.

I am, Sir, yours faithfully,

W. M. CROFTON.

University College, Dublin, Oct. 7th, 1929.

HARMINE OR HYOSCINE FOR ENCEPHALITIS.

To the Editor of THE LANCET.

SIR,—In your issue of Sept. 28th (p. 647) Dr. T. R. Hill and Dr. C. Worster-Drought discuss the treatment of chronic encephalitis with harmine and contrast their results with those reported by Rustige in Germany. Although Rustige does not claim that his findings bring harmine within the range of practical therapeutics, yet the discrepancy between his observations and the more recent ones remains to be accounte l for. May it not rest upon the form and duration of the previous treatment that these different groups had undergone? The cases reported in your columns had been treated with hyoscine hydrobromide gr. 1/100 hypodermically three times daily, for how long is not stated. Rustige's patients had been treated with "scopolamine-atropine," how much or how long again we are not told. Hyoscine, I think, has a greater psychical effect than atropine, habit is more readily established, and in some cases it seems that its influence is very largely subjective. Under the circumstances and in default of fuller information it seems reasonable to suggest that the patients of Hill and Worster-Drought had become more dependent on the treatment in force before the change than were those of Rustige. The insistence of the encephalitic who is under treatment by hyoscine on his need for hyoscine seems to offer a serious obstacle to successful results with any alternative. He is acutely aware of all his objective manifestations, and if he believes that hyoscine keeps them in abeyance he may quite conceivably recall every one when his hyoscine is withdrawn, for his memory of detail is far better than that of the general run of patients. That there should be, as Drs. Hill and Worster-Drought describe, a rapid improvement on resumption of hyoscine does not negative this suggestion.

I am, Sir, yours faithfully,

Dundee, Oct. 3rd, 1929. J. M. STALKER.

LIVER TREATMENT IN SUBACUTE COMBINED DEGENERATION OF THE CORD.

To the Editor of THE LANCET.

SIR,—In his review of the nervous and mental aspects of pernicious anæmia (THE LANCET, Sept. 28th, p. 643), Dr. Douglas McAlpine criticises an article by Dr. M. M. Suzman and myself on subacute combined degeneration of the cord. While in agreement with him that the type with pyramidal involvement and little anæmia is more resistant to liver treatment, we have found that many of the spastic cases with marked anæmia have done very well indeed. We have re-examined our cases after an average period of 16·6 months' liver treatment, and in two further cases, making five in all, extensor plantar responses have become flexor in type. We have had no occasion to modify our opinions as to the good results obtained in subacute combined degeneration with sufficient liver dosage, provided that there is no urinary or dental sepsis. It is essential, however, that the cases be followed up for a sufficient length of time, as the effects on the nervous system may not be apparent for months after the anæmia has disappeared. It must be emphasised also that the optimum amount of liver required for improvement in the nervous phenomena is considerably in excess of the minimum amount required to combat the anæmia.

Dr. McAlpine wishes to draw conclusions with regard to the degree of anæmia in our non-improved cases. A careful study of the article will render it obvious that the reasons for failure to improve in these were, not the absence of a marked anæmia, but the inadequate dosage of liver, and in some the presence of septic complications. We have not found the administration of hydrochloric acid to affect the rate of improvement; the majority of our improved cases had none. Its use, however, has been found beneficial at times for gastric symptoms.

In conclusion, may I point out an error on p. 646 in quoting our report. The sentence (col. 2, line 34) should read, "of the 31 cases that had no liver, 28 died within an average period of 14·6 months (not 4·6 months) from the onset of the disease."

I am, Sir, yours faithfully,

C. C. UNGLEY, M.D., M.R.C.P.

Newcastle-on-Tyne, Oct. 4th, 1929.

ABDOMINAL TENDERNESS AND UNNECESSARY OPERATIONS.

To the Editor of THE LANCET.

SIR,—In the note on this subject, on p. 740 of your last issue, your occasional correspondent in the United States describes Dr. J. B. Carnett's teaching as "certainly heretical." I am amazed at this late date to find such a statement in print. I have held these views and used the same tests as Dr. Carnett for some years, and find that the condition he describes is very prevalent. Because tender nerve segments occur in the abdomen and chest the profession, as a whole, have accepted the work of Head and Mackenzie as interpreting that the disturbance is due to disease in one or other organs innervated by that spinal segment. If, however, the pains are complained of in an extremity, then the diagnosis is neuralgia or neuritis!

I am, Sir, yours faithfully,

R. CHALMERS, M.D., F.R.C.S.E.

Darlington, Oct. 4th, 1929.

TRELOAR CRIPPLES' HOSPITAL.—The work of replacing the wooden wards at Alton has now begun. There are to be five ward blocks of 60 beds each, and each ward unit provides for two wards of 24 beds each, two wards of four beds each, and four cubicles. They will face south to a wide terrace nearly 1000 feet long, and the large wards will have folding doors to enable them to be used as open-air wards opening upon a verandah glazed with Vita-glass. The administrative block will be on the north side.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION.—The opening lecture of a series on Common Complaints will be delivered by Dr. F. G. Chandler on Monday, Oct. 14th. Particulars of this and other lectures during the coming week will be found in our Medical Diary. Sixteen lectures intended for candidates for the M.R.C.P. examination will be held at 8.30 P.M. on Tuesdays and Fridays, from Oct. 15th to Dec. 6th, at the rooms of the Medical Society of London. From Oct. 14th to 26th a morning course will be given at the Hospital for Sick Children, and between the same dates there will be a course in gynæcology at the Chelsea Hospital. An intensive course will be held at the Central London Throat, Nose and Ear Hospital from Oct. 14th to Nov. 2nd; and an intensive course in medicine, surgery, and the specialties at the Metropolitan Hospital from Oct. 21st to Nov. 2nd. The latter course is intended to appeal to practitioners. Further information about special and general courses may be had from the Secretary of the Fellowship at 1, Wimpole-street, London, W.1.

Obituary.

THOMAS JENNER VERRALL, M.R.C.S. ENG., LL.D. ABERD.,

LATE CHAIRMAN OF REPRESENTATIVE BODY, BRITISH MEDICAL ASSOCIATION.

WE regret to announce the death on Oct. 4th of Sir Jenner Verrall, one of the best-known workers in the country for the advancement of the whole medical profession.

Thomas Jenner Verrall was born in 1852 at Brighton, the second son of Henry Verrall, a well-known Brighton solicitor, his elder brother being Arthur Woollgar Verrall, the famous Cambridge Greek scholar. Jenner Verrall was educated at Marlborough, and on leaving school in 1869 proceeded to St. Bartholomew's Hospital, whence he duly qualified in 1876. He had previously gone through a part of his medical training at the Sussex County Hospital, and shortly after qualification was elected surgeon to that institution, a post which he held until 1912, when he was elected consulting surgeon. As a practitioner he won from the start the esteem and confidence of a large circle of patients and friends, and when, not long before the outbreak of war, he retired to Bath, at the age of 60, he set himself to further assiduously and assist practically the development policy of the British Medical Association, which had its origin in the reconstitution of that body in 1902. He had already for ten years studied the interests of the Association in connexion with the medical profession at large, had been elected to the Council and discharged many local responsibilities, and now the leisure of retirement gave him further opportunities of working along lines he loved.

To enumerate the many committees of the Association upon which he served would become tedious from the mere length of the list; it must suffice to say that wherever the conduct of medical practice came into contact with the constitutional or social life of the country to an extent that warranted the institution of a committee for the collection of information or the furtherance of reform, Verrall was always a prominent member of that committee. And to all the varying subjects which thus came within his ken he contributed sagacious counsel which gained in acceptance from the possession of a winning manner, a command of witty words, and obvious sincerity. A member of the Council of the Association since 1893, from 1913 to 1915 he was chairman of the Representative Body, and while occupying that responsible post he was the recipient of the gold medal of the Association in acknowledgment of his services. Of his multifarious Association committees he was at different times chairman of the Organisation, the Medico-Political, and especially of the State Sickness Insurance and the Central Medical War Committee, and his work on the last two was prominent. The institution of national insurance, owing to the sharply divided opinions, both on principle and in detail, as to the merits and demerits of the new legislation, placed the medical profession, and especially the British Medical Association, in a difficult position; while it was felt at the time that the Association was especially fortunate in having a competent body of men prepared to deal with the recurring professional difficulties, among whom none earned, or deserved, higher credit than Verrall and the late Dawson Williams. The Insurance Acts were not in working order when the war broke out, and almost immediately it was realised that much of the available strength of the medical profession would have to be used, and used over a considerable period, for military service, largely with the forces abroad, while the maintenance of the general health of the country was as necessary for the carrying on of hostilities as for the preservation of social conditions. The problem briefly was how far it would be possible to denude the country of medical service while preserving a level of general safety, and how at the same time to use those who, by economical arrangement could be set free for military objects, in the most efficient way. A prompt and fair arrangement of recruiting had to be instituted, and to this end the Central Medical War Committee was formed, as a medium between the medical profession on the one hand and, on the other, the War Office and the home population. The circumstances of each locality, and of each medical man residing therein, were inquired into, and as prompt and fair way as possible under which to adjust national claims and individual rights was arrived at. Verrall was chairman of the Committee, and presided over its deliberations with firmness and tact, conducting its complicated business with an expedition that was necessary, even while he showed himself ready in all circumstances to provide a clear and detailed explanation of any decision at which the Committee arrived. At the close of the war his energy and industry were rewarded with a well-won knighthood.

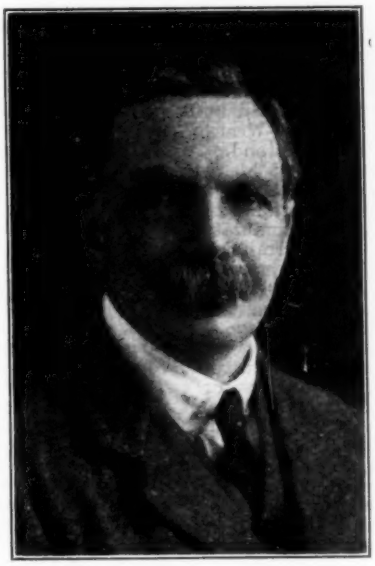
Verrall was first elected a Direct Representative for England and Wales on the General Medical Council in 1911, occupying thus a seat on that body for the unusual duration of 18 years. In discharging his duties on the Council he was never forgetful that he represented the medical profession as a whole and not the Association, and the vote of thanks which was accorded to him at the last meeting of the Association, upon his retirement from the Council, was in accord with a universal feeling in the profession that he had served the public, as well as his own calling, admirably in many important and responsible capacities.

His death occurred, at the age of 77, at East Lodge, Leatherhead, where he had lived for some years.

WILLIAM GORDON, M.D. CAMB., F.R.C.P. LOND.,

LATE SENIOR PHYSICIAN TO THE ROYAL DEVON AND EXETER HOSPITAL.

ON Oct. 1st, at a nursing home in Exeter, the well-known physician, William Gordon, died as a sequel to a severe attack of influenza in his sixty-seventh year. He was known for his scientific equipment and his zealous pursuit of knowledge, not only in the West of England, but throughout the country.



DR. WILLIAM GORDON.

William Gordon was born at Strabane in 1863, son of Mr. George Gordon, J.P., and was educated privately with such good effect that he entered Trinity College, Cambridge, with an exhibition which was later transformed into a scholarship. He justified his boy's promise by securing a first-class in both parts of the Natural Science Tripos, and later pursued his medical studies at University College Hospital, where he was a house physician, and Heidelberg. He qualified as M.B., B.Chir. Camb. in 1890, became M.R.C.P. Lond. in 1891, proceeded to the doctorate in 1894, and in 1903 was elected F.R.C.P.

Gordon commenced medical practice in Exeter, the city in which he passed all his professional life. Early elected to the staff of the Royal Devon and Exeter Hospital, he held also in the Exeter area the posts at various times of physician to the West of England Eye Infirmary and physician to the Exeter Dispensary. His learning and keenness commanded, almost from the beginning, a large domestic and consulting practice, while as a climatologist he was known throughout the scientific world. His deep interest in the subject of tuberculosis was closely associated with his views upon the interplay of meteorological conditions with the incidence of disease. Some of the conclusions which he arrived at were bold, and did not escape challenge, but his investigations into the cause and effect of phthisis in the western counties, and his intensive study of the connexion between the ravages of the disease and the prevalence of certain atmospheric conditions, brought up for consideration many points which too often escape attention. He was as enthusiastic here as he was on the subject of the diagnosis of cancer, and, like all enthusiasts, he made statements which were rather the result of personal belief than of actual proof, but of his intellectual capacity and of his complete sincerity none of his critics had ever any doubt. The Samuel Hyde Lectures on the Place of Climatology in Medicine, delivered in 1913 before the Balneology and Climatology Section of the Royal Society of Medicine, contain in brief his views on a many-sided subject; these were published in THE LANCET on delivery, and were recognised by readers as containing much valuable and suggestive teaching.

Gordon took an active part in the affairs of the British Medical Association, was President of the Section of Medicine at the annual meeting in 1907, and, in particular, was Chairman of a Subcommittee on Army Reform, a subject which deeply interested him. In this connexion, indeed, he is known to have given the late Lord Lansdowne, then Secretary of State for War, much support during the erection of the Army Medical Service into the Royal Army Medical Corps.

Dr. F. A. ROPER sends us for publication the following tribute to his dead friend: "I am glad of this opportunity to pay sad respect to the memory of one whom I have known all my life, and who has been my colleague at the Royal Devon and Exeter Hospital for 16 years. The grief following the loss of one who, during 38 years of active service for the hospital, had built up a commanding reputation in the South-West of England as a physician will readily be understood. At the bedside the dominant characteristic of his work was thoroughness and, arising from that, an earnest striving for precision; and, examination completed, it was then that the knowledge accumulated by his wide experience and lifelong and unremitting study showed themselves. For Gordon remained a student devoted to his books till the very end, and even more intensively so after his retirement from the active staff of the hospital 15 months ago. For his hospital work ever received from him a generous share of his time, and it was no unusual occurrence for him to visit an individual patient daily, or twice daily, where there was any doubtful or difficult problem of diagnosis or treatment to be faced. And his conscientiousness was at once revealed and illustrated to anyone who saw the classified records he kept for his own use of hospital and private cases alike. As a colleague the strength of his firmly marked and impulsive personality showed itself in an unswerving loyalty to, and care for the prestige and honour of his profession, a loyalty which at times evoked criticism by the very forcefulness of its expression; but, ever impatient as he was of opposition, this daunted Gordon not at all, but rather acted as a spur to increased earnestness. As a junior colleague, and friend of his in the personal sense, I can testify that during many years spent in intimate touch with him, frequently over difficult and controversial hospital and private problems, I never on any single occasion experienced from him any but the most scrupulous courtesy, kindness, and encouragement. He ever gave of his best, as the devotion and reliance he commanded of his patients further testified. His intellectual activities outside his profession covered a remarkably wide range. He was an enthusiastic and deeply-read historian, with an extremely retentive memory for facts; a student of architecture; and possessed a considerable degree of artistic ability. Until latterly he was a keen musician, and among his more intimate friends was known as a pianist of sympathetic touch and considerable interpretative insight; while in another direction his book of poems on the war—produced for private circulation only—evidenced among many other traits his admiration and respect for the private soldier. His literary ability was further displayed in his beautifully phrased concise speeches at gatherings, both scientific and social, and his scholarly attainments and methods generally make the gap caused by his loss one that will be felt for many a long day to come. With us his name has been a household word."

Dr. Roper's words set out Gordon's striking characteristics, and the accompanying portrait, taken in middle life, agrees with them.

The grief in Exeter and the surrounding district was accentuated by the unexpected termination to an attack of influenza, as Gordon was carrying on practice in his customary good health until quite recently. He leaves a widow, and an only son of 25, who is in India.

The Services.

ROYAL NAVAL MEDICAL SERVICE.

THE following appointments are notified: Surg. Lt.-Comdr. T. N. D'Arcy to *Warspite* (on transfer of flag); and Surg. Lts. L. J. Corbett to *Warspite* and L. P. Spero to *Queen Elizabeth* (on transfer of flag).

ROYAL ARMY MEDICAL CORPS.

Bt. Lt.-Col. F. D. G. Howell to be Asst. Dir.-Gen., Army Med. Servs., War Office, vice Col. W. R. P. Goodwin (vacated).

Maj. W. R. O'Farrell retires on retd. pay.

Capt. A. R. Barlas to be Maj.

Capt. W. Parsons, late R.A.M.C., is granted a temp. commn. in the rank of Capt.

TERRITORIAL ARMY RESERVE OF OFFICERS.

Lt.-Col. J. E. H. Sawyer, having attained the age limit, relinquishes his commn. and retains his rank.

ROYAL AIR FORCE.

Flight Lt. E. J. Jenkins resigns his permanent commission.

INDIAN MEDICAL SERVICE.

Maj. Gen. W. H. S. Nickerson, V.C., late R.A.M.C., to be Dir. Med. Services, India.

COLONIAL MEDICAL SERVICES.

The following appointments are notified: Dr. P. D. Johnson and Dr. J. E. McMahon, Medical Officers, Federated Malay States; Dr. A. W. H. Smith, Assistant Medical Superintendent, Tonjong Rambutan Central Mental Hospital, Federated Malay States; Dr. L. B. Haye, Medical Officer, and Dr. A. W. Rose, Pathologist, Nigeria; and Dr. E. J. Thomas, Medical Officer, Northern Rhodesia.

The following appointments in the West African Medical Staff have also been notified: Dr. G. W. Aynes, Dr. W. C. Davidson, Dr. C. N. Latham, and Dr. C. H. C. White, Medical Officers, and Dr. J. C. B. Craig and Dr. A. D. Cust, Medical Officers of Health.

THE King has granted permission to Lieut.-Colonel Sir Charles H. Bedford, I.M.S. (retd.), to accept and wear the insignia of Knight Grand Cross of the Order of Civil Merit of Spain, conferred upon him by the King of Spain. We understand that the only other British subjects who have received this honour are the Maharajahs of Patiala and of Kapurthala, on the occasion of their State visits to Madrid last year. Apart from other services to Spain for several years past, Sir Charles Bedford originated the King Alfonso XIII Chair of Spanish Studies at the University of Oxford in 1926, commemorating the Prince of Wales's visit to Spanish South America.

Medical News.

UNIVERSITY OF LIVERPOOL.—At recent examinations the following candidates were successful:—

D.P.H.

J. L. Clegg, R. L. Corlett, R. W. Eldridge, A. B. Follows, B. S. Jarvis, J. C. McVittie, R. J. Ormsby, D. E. P. Pritchard, D. Regan, and F. C. Speechly.

THE RED CROSS AND MUSTARD GAS.—The International Committee of the Red Cross offers a prize of 10,000 Swiss francs for a reagent capable of distinguishing without any ambiguity the presence of mustard gas in a concentration of 0·07 mg. per litre of air. The reaction should be characteristic and the reagent and the apparatus submitted should be simple to manufacture and moderate in price when turned out in large quantities. The jury which will decide on the award of the prize will consist of Prof. F. Haber, of Berlin, Sir William J. Pope, F.R.S., of Cambridge, Prof. M. F. Swarts, of Ghent, and Prof. M. G. Urbain, of Paris. Competitors must send their proposals in proper form to the Secretary of the International Committee of the Red Cross, in Geneva, before Dec. 31st, 1930. The reagent adopted will be called by its author's name and will become the property of the International Red Cross.

CHARING CROSS HOSPITAL POST-GRADUATE COURSE. A successful week-end post-graduate course was held in the Medical School on Oct. 5th and 6th, more than a hundred former students of the hospital attending. On Oct. 5th, in the morning, Mr. H. S. Clogg opened the course with a lecture on Diseases of Gall-bladder, and was followed by Mr. Bright Banister on Some Obstetric Difficulties, and by Dr. D. Forsyth on Some Everyday Neuroses. In the afternoon Mr. P. L. Daniel lectured on Common Ailments of the Rectum; Dr. F. G. Chandler on Puncture of the Chest: Its Occasions and Technique; and Dr. J. M. H. MacLeod on Tuberculosis of the Skin. On Sunday, Oct. 6th, the lectures given were as follows:—Mr. H. E. Batten: Fractures. Dr. Gordon Holmes: Syphilis of the Nervous System. Mr. Norman Lake: Injection Treatment of Varicose Veins. Dr. Howard Jones: A Short Review of Anæsthetic Practice. Dr. W. J. Adie: Early Symptoms of Some Common Nervous Disorders. Mr. E. D. Davis: Ear, Nose, and Throat Work in General Practice.

CHARING CROSS HOSPITAL DINNER.—The annual dinner of past and present students coincided with the first week-end post-graduate course ever held at the hospital, and was for this reason more than usually well attended. Nearly 160 covers were laid at Gatti's Restaurant on the evening of Oct. 5th when Dr. J. M. H. MacLeod took the chair and the toast list was agreeably short in order to give time for an admirable programme of music arranged by Dr. Taylor Harris. Mr. Norman Lake, in proposing "Hospital and Medical School," spoke of the completion of the additional wing which would relieve the general wards of overcrowding by providing a complete unit for the skin, orthopædic, dental, and other departments. Mr. J. Bright Banister, who replied in the absence, through illness, of the Dean, Dr. F. H. Young, recounted the signs of prosperity in the school and the prospect of an increasing number of students. Dr. W. C. Bosanquet proposed "The Chairman," who made a graceful reply. Among the items in the musical programme were three songs by Dr. Harris himself rendered with refreshing vigour and faultless technique, and a version, by Mr. Nelson Jackson, of Hamlet describing a cocktail.

ST. THOMAS'S HOSPITAL DINNER.—The annual dinner was held on Oct. 4th at St. Thomas's House, with Dr. H. G. Turney in the chair. There was an attendance of old students to the number of nearly 200, of every degree of seniority, who evidently appreciate the amenity of being able to meet and dine together in their own house. Among the invited guests were the Directors-General of the three medical services, the President of the Royal College of Physicians, the medical officer of health and the coroner for the area, a representative of London University, the headmaster of the Merchant Taylors School, and the architect of the new building. Dr. Turney, in proposing "Hospital and Medical School," opened with an amusing dissertation on doctors who are not doctors, but have deviated before or after qualification into one or other of the pleasant by-ways of life. He noted the curious fact that after being patron saint of the hospital for 300 years Thomas à Becket had been supplanted by the apostle of that name, and he pleaded with the treasurer for the restitution of the all-British patron. The partial eclipse consequent on the transplantation of the ancient hospital from the borough to its present site had, he felt, now fully disappeared. Sir Arthur Stanley, in replying, offered to look round for the best saint of the name, and spoke of the past year as one of extreme importance in the history of the hospital. For 12 years past he had been receiving demands on every hand for more accommodation. They were not allowed to build bridges, to approach the new site on the south side of Lambeth Palace-road, and tunnels must be so deep as to run the risk of flood. The new scheme would therefore transplant the medical school so as to build in its place a worthy out-patient department adjoining the wards. A joint appeal was shortly to be issued for certainly not less than £500,000, in the collection of which he looked hopefully to the aid of St. Thomas's men. The Dean, Prof. L. S. Dudgeon, replied for the medical school, sketching in a few sympathetic words the careers of the great men who had been lost to the school in the past year—Sharkey, Mackenzie, Caiger, George Maling, V.C., E. L. Atkinson, R.N., a member of Scott's expedition—and passing on to those retiring from the staff, especially Dr. J. S. Fairbairn, a man of ideas, a first-rate teacher and organiser, and a fine physician. Dr. H. Yellowlees had succeeded Dr. W. H. B. Stoddart, Prof. S. J. Cowell had delivered his first course on dietetics, Sir George Makins had received the honorary gold medal of the Royal College of Surgeons, a worthy successor of Lister and Paget. Finally he remarked that the new medical school would be six storeys in height, would cost £220,000, and would contain on the top 24 bedrooms supplementary to those in St. Thomas's House. Sir Percy Sargent proposed "The Guests," and Sir John Rose Bradford replied; it was, he said, a pleasing feature to entertain guests from other schools who had not much opportunity of meeting. The toast of "The Chairman" was proposed by Dr. A. E. Russell, who spoke of the service which Dr. Turney, after ten years of retirement, was still rendering to the hospital in his attendance on the nursing staff and as an almoner. The dinner concluded with the presentation of an illuminated address and a cheque to the school bedell, whose service with that of his father and grandfather covered a period of over 100 years.

ST. GEORGE'S HOSPITAL DINNER.—The annual dinner of the hospital and medical school was held on Oct. 1st at the Hyde Park Hotel with Dr. Digby Cotes-Preedy, K.C., in the chair. More than 100 past and present St. George's men attended, and a most enjoyable evening was spent. In reply to the toast of the "Hospital and Medical School" the Dean, Dr. Anthony Feiling, stated that the school had had a successful year, and that an excellent entry of new students was assured. The health of "The Chairman" wittily proposed by Mr. Ivor Back was replied to in like vein.

ST. MARY'S HOSPITAL DINNER.—Sir John Broadbent presided at the annual dinner at the Trocadero Restaurant on Oct. 4th, when the toast of "St. Mary's Hospital and Medical School" was proposed by Lieut.-Colonel H. E. Verey, as chairman of the Hospital Board. After referring to the large sums the School had received by the gift of Lord Beaverbrook and the bequest of Lord Revelstoke, Colonel Verey said it was hoped that rebuilding would begin early next year. If possible, work would start at the same time on the new inoculation department, for which Lord Iveagh's generous donation of £25,000 over a period of seven years would bring in a total of about £40,000. On the site of the old medical school a nurses' home would be built to accommodate four or five hundred, whilst the present nurses' home would provide ideal accommodation for paying patients—a most urgent necessity. The extensions of the hospital coming into operation this year had cost £63,000, of which £62,000 had been raised. The operating theatres were now as modern as any in the country, and the increase in the number of beds would mean better service for the locality. Colonel Verey congratulated the School on winning the Inter-hospital Cricket Cup, which had been absent since 1899. He went on to pay a tribute to Mr. Warren Low, whom he described as a tower of strength to the Hospital Board. He trusted that after Mr. Low's retirement from the surgical staff in November the Board would continue to enjoy his wise advice and tactful help. Another resignation which would be deeply regretted was that of Mr. Leslie Paton from the post of ophthalmic surgeon. In his reply, Dr. C. M. Wilson, the Dean, said it had been a wonderful year for the School, whose record, indeed, during the last ten years had been a romance. The late war had made the task of every medical school very difficult: expenses had been quadrupled, whilst income remained the same. Those who held that there were too many medical schools had welcomed this situation because they thought it would eliminate the weakest, but it was remarkable that the two most threatened with destruction—namely, the Middlesex and St. Mary's—were the two which had gone ahead most of all in recent years. St. Mary's had secured £150,000 for new school buildings, and hoped to get the remainder needed. They were out to make it the best school in London—best not because it had the best buildings

or even the best staff, but because it had the best students. Sir John Broadbent, whose health was drunk with musical honours, responded entertainingly to the toast, and took occasion to recall the merits of many of his colleagues. The proceedings closed with a speech from the captain of the cricket team, the health of which was proposed by the chairman.

MEDICAL SICKNESS, ANNUITY, AND LIFE ASSURANCE SOCIETY, LTD.—The annual meeting of this Society was held on Oct. 7th under the chairmanship of Dr. F. J. Allan. The chairman in his address stated the report showed the Society had had a successful year. The premium income in the Sickness Fund was now £60,700. The sickness claims paid had increased from £31,000 to £38,196, chiefly on account of the influenza epidemic, for which claims were paid amounting to £6200. The total of the funds at the close of the year was £383,761. New life assurance policies were issued for £243,460 gross, and the funds had increased to £222,722. The total premium income of the Society was £98,050, and expenses of administration £13,348. The management expenses showed a gratifying fall in the ratio to premium income from 13·8 per cent. to 13·4 per cent. The gross rate of interest earned over the whole funds was £5 0*s.* 3*d.*, and net rate £4 3*s.* 2*d.* Dr. Allan stated that the investments of the Society were in a sound condition, and the auditors certified that the market prices of the stocks at June 30th, 1929, were £11,786 in excess of the values stated in the balance-sheet. The total funds of the Society now amounted to £628,588.

Dr. Harvey Hilliard, in moving three resolutions in respect of permanent sickness insurance contracts to age 70, fixing the date of the annual meeting, and printing and publishing a list of members, said that when he sent these to the office to be placed on the agenda of the meeting he was informed that they were matters arising out of the report, but he maintained that this was not the correct procedure. The chairman replied that he was informed by the legal advisers of the Society that the procedure adopted was in accordance with that usually adopted by other companies, but that the Board was prepared to consider a scheme for extending permanent sickness insurance to age 70. In the matter of fixing the date of the meeting, it was decided that the date should be published in the medical press six weeks beforehand. The motion for publishing a list of members being put to the meeting was lost by a large majority. The report was adopted, and the two retiring directors, Sir William Willcox and Mr. W. H. Dolamore, were duly re-elected. Dr. Harvey Hilliard's motion that all directors of the Society should retire at age 65 was withdrawn by him. After a vote of thanks had been unanimously passed to Dr. Allan the meeting closed.

GRESHAM LECTURES.—Four lectures on How England Learned to Control Disease will be given by Sir George Newman at 6 P.M. on Oct. 15th, 16th, 17th, and 18th, at Gresham College, Basinghall-street, London, E.C.

GUILD OF ST. LUKE.—The Annual Medical Service will be held at Westminster Abbey on Sunday, Oct. 20th, at 6.30 P.M., when the Bishop of Bradford will be the preacher. Medical men, women, and students are invited to attend. Those wearing academic dress will not require tickets, but will proceed to the Jerusalem Chamber and robe there. Tickets for others and their friends may be had from the Secretary of the Guild, King's College, Strand, London.

NATIONAL COUNCIL FOR MENTAL HYGIENE.—A conference on mental health will be held in the Central Hall, Westminster, from Oct. 30th to Nov. 2nd. The subjects to be discussed include Sex Education, the Personal Equation in Industry, the Child and the Parent, and Delinquency. There will also be group discussions on the Working of the Juvenile Courts, the Relation of the Work of Public Health Nurses and Social Workers to the Mental Health of the Community, and the Problem Child at Home and in School. Further particulars may be had from the Secretary of the Council, 78, Chandos House, Palmer-street, London, S.W. 1.

BRITISH SCIENCE GUILD.—The Norman Lockyer Lecture for 1929 will be given at the Goldsmiths' Hall, Foster-lane, London, E.C., at 4.30 P.M., on Tuesday, Nov. 19th, by Sir Walter Fletcher, F.R.S., Secretary of the Medical Research Council, who will speak on certain aspects of medical research and their applications.

A lecture has been established in memory of Sir Alexander Pedler, F.R.S., who was for many years honorary secretary of the Guild. The first Alexander Pedler Lecture will be given at Manchester, at 5.30 P.M., on Nov. 26th by Mr. G. C. Simpson, F.R.S. The subject will be Past Climates, and the lecture will be held under the auspices of the Manchester Literary and Philosophical Society at 36, George-street.

POST-GRADUATE COURSE ON ORTHOPÆDICS.—A fortnight's course will be held at the Royal National Orthopædic Hospital, London, from Nov. 18th to 30th. Particulars will be found in our advertisement columns.

INTERNATIONAL LEAGUE AGAINST TRACHOMA.—At the International Ophthalmological Congress recently held in Holland (see THE LANCET, Sept. 21st, p. 633) it was resolved to form an International League against Trachoma. Prof. Emile de Grósz, of Budapest, was elected president, and Dr. F. Wibaut, of Amsterdam, secretary, and they were entrusted with the formation of a committee from among the delegates of the ophthalmological societies and leagues already in existence. Prof. de Grósz's address is Baross-u., 10, Budapest VIII.

INFECTIOUS DISEASE IN ENGLAND AND WALES DURING THE WEEK ENDED SEPT. 28TH, 1929.

Notifications.—The following cases of infectious disease were notified during the week:—Small-pox, 108 (last week 119); scarlet fever, 2590; diphtheria, 1367; enteric fever, 101; pneumonia, 720; puerperal fever, 46; puerperal pyrexia, 86; cerebro-spinal fever, 10; acute poliomyelitis, 37; acute polio-encephalitis, 4; encephalitis lethargica, 12; continued fever, 1; dysentery, 11; ophthalmia neonatorum, 106. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the Metropolitan Asylums Board on Oct. 1st–2nd was as follows:—Small-pox, 143 under treatment, 10 under observation (last week 122 and 19 respectively); scarlet fever, 1738; diphtheria, 1764; enteric fever, 18; measles, 172; whooping-cough, 196; puerperal fever, 24 (plus 8 babies); encephalitis lethargica, 125; poliomyelitis, 5; "other diseases," 13. At St. Margaret's Hospital there were 19 babies (plus 9 mothers) with ophthalmia neonatorum.

Deaths.—In the aggregate of great towns, including London, there was no death from small-pox, 3 (0) from enteric fever, 12 (2) from measles, 6 (0) from scarlet fever, 15 (3) from whooping-cough, 31 (9) from diphtheria, 186 (36) from diarrhœa and enteritis under two years, and 23 (5) from influenza. The figures in parentheses are those for London itself.

Of the deaths from diarrhœa (which have increased by a bare quarter), 31 were reported from Birmingham, 18 from Liverpool, 12 from Sunderland, 11 from Hull, 8 from Manchester, 7 from Middlesbrough, and 6 from West Ham; while Glasgow, Dublin, and Belfast reported 15, 8, and 7 respectively. The deaths from enteric fever were reported from Wimbledon, Newcastle-on-Tyne, and Swansea.

The number of stillbirths notified during the week was 236 (corresponding to a rate of 35 per 1000 births), including 43 in London.

Medical Diary.

SOCIETIES.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.

MONDAY, Oct. 14th.—5 P.M., WAR. Presidential Address by Group-Captain Hardy V. Wells, R.A.F.

TUESDAY.—8 P.M., PATHOLOGY. Prof. A. E. Boycott: The Blood as a Tissue (Presidential Address). 8.30 P.M., ORTHOPÆDICS. Dr. Fred Albee (New York) will give an Address on Original Surgical Applications of the Bone Graft, illustrated by lantern slides and moving pictures. Members of the Section of Surgery are cordially invited to attend.

WEDNESDAY.—8 P.M., TROPICAL DISEASES. Dr. G. Giglioli: Paratyphosus Infections in British Guiana—Sterile abscess in Treatment—Demonstration of Specimen. Dr. W. Broughton-Alcock: Section Showing Structures Morphologically Resembling Spirochætes of a Species Common to the Mouth, lying deep within its mucous membrane (for opinion).

THURSDAY.—5 P.M., DERMATOLOGY. (Cases at 4 P.M.)

FRIDAY.—8 P.M., OBSTETRICS, COMPARATIVE MEDICINE. Special Discussion on Causes of Early Abortion and Sterility. Openers: Prof. A. Robinson and Prof. Beckwith Whitehouse (Obstetrics); Mr. J. R. Barker and Mr. O. Stinson (Comparative Medicine). 8.30 P.M., ELECTRO-THERAPEUTICS. Presidential Address by Dr. C. A. Robinson.

MEDICAL SOCIETY OF LONDON, 11, Chandos-street, Cavendish-square, W.

MONDAY, Oct. 14th.—8 P.M., Annual General Meeting. 8.30 P.M., Mr. Donald Armour: Some of Lettsom's Contemporaries (Presidential Address).

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 11, Chandos-street, Cavendish-square, W.
THURSDAY, Oct. 17th.—7.45 P.M., Demonstration of some of Dr. Low's Original Preparations showing the Development of Filariæ in Mosquitoes.—8.15 P.M., Dr. G. Carmichael Low: A Retrospect of Tropical Medicine from 1894–1914 (Presidential Address).

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.
FRIDAY, Oct. 18th.—5 P.M., Sir Arthur Keith: Specimens of Trephining—Ancient and Modern.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.
MONDAY, Oct. 14th, to SATURDAY, Oct. 19th.—MEDICAL SOCIETY OF LONDON. Mon., 5 P.M., Dr. F. G. Chandler: The Treatment of Pulmonary Tuberculosis. No fee. Tues., 8.30 P.M., Dr. Parsons-Smith: The Symptoms and Signs of Myocardial Failure. Fri., 8.30 P.M., Dr. Parsons-Smith: The Treatment of Heart Disease. ST. JOHN'S HOSPITAL FOR DISEASES OF THE SKIN. Mon. 2 to 4 P.M., Dr. W. Griffith: Demonstration. No fee.—SAMARITAN HOSPITAL, Marylebone-road, N.W. Thurs., 2.30 P.M., Mr. Andrew McAllister: (Gynæcology) Demonstration. No fee.—HOSPITAL FOR TROPICAL DISEASES, 25, Gordon-street, W.C. Tues. and Thurs., 2 P.M., Lecture-demonstrations by Dr. Manson-Bahr and Dr. Carmichael Low.—CHELSEA HOSPITAL, Arthur-street, S.W. Special Courses in Gynæcology for two weeks.—HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C. Special morning course.—CENTRAL LONDON THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C. Intensive Course. Further particulars from the Fellowship of Medicine.

LONDON HOSPITAL POST-GRADUATE COURSE.
WEDNESDAY, Oct. 16th.—10.15–10.45 A.M., Dr. Russell Brain: The Therapeutic Uses of Luminal. 11–11.30 A.M., Dr. W. W. Woods: The Causes of Sudden Death (with specimens). 11.30–11.45 A.M., Dr. S. Phillips Bedson: Recent Work on Vaccination. 12–12.45 P.M., Mr. Hugh Lett: Hæmaturia. 1.30–2 P.M., Sir R. S. Woods: The Present Position of General Light Therapy. 2–3 P.M., Mr. W. S. Perrin: Demonstration of Cases Treated by Radium. 2–4 P.M., Mr. E. C. Lindsay: Surgical Operations. 2–3.30 P.M., Dr. George Riddoch: Demonstration of Neurological Cases. 3.45–4.30 P.M., Dr. John Parkinson: Non-valvular Diseases of the Heart (Cases and Lantern slides).
THURSDAY.—10–10.45 A.M., Dr. W. J. O'Donovan: Occupational Dermatitis (Lantern Demonstration). 11–11.45 A.M., Dr. Maitland-Jones: Infant Feeding. 11.55 A.M.–12.10 P.M., Dr. Donald Hunter: Modern Treatment of Lead Poisoning. 12.15–12.45 P.M., Mr. Alan Perry: Injection Treatment of Varicose Veins (Lecture and Demonstration). 1.30–2 P.M. Mr. H. S. Souttar: Radium and Its Surgical Application. 2–3.30 P.M., Mr. Souttar: Surgical Operations; Dr. R. A. Rowlands and Mr. J. D. Driberg: Ward Demonstrations. 3.45–4.30 P.M., Dr. O. Leyton: Diabetes.
FRIDAY.—10–10.45 A.M., Prof. A. W. M. Ellis: Use and Abuse of Intravenous Therapy. 11–11.45 A.M., Dr. P. N. Panton: Pernicious Anæmia. 12–12.45 P.M., Mr. Robert Milne: Pain in the Fore Part of the Foot. 1.30–3.30 P.M., Mr. A. J. Walton: Operations. 1.30–2.30 P.M., Dr. A. E. Clark-Kennedy: Cardiac Pain (Ward Demonstration). 2.30–3.30 P.M., Dr. Theodore Thompson: Ward Demonstration. 3.45–4.30 P.M., Mr. Eardley Holland: Uterine Hæmorrhage (Gynæcological Demonstration). 9 P.M., Dr. Ashley Daly: Methods of Anæsthesia (Demonstration).
SATURDAY.—10–10.45 A.M., Dr. Robert Hutchison: Dyspepsias of Childhood. 11 A.M. to 12 noon, Mr. Russell Howard: Ward Demonstration. 12–12.45 P.M., Mr. Walton: Place of Surgery in Lesions of the Stomach.

NATIONAL HOSPITAL, Queen-square, W.C.
MONDAY, Oct. 14th.—12 noon, Dr. Greenfield: Pathology of Nervous System. 2 P.M., Dr. Riddoch: Out-patient Clinic. 3.30 P.M., Dr. Adie: Disseminated Sclerosis.
TUESDAY.—2 P.M., Dr. Walshe: Out-patient Clinic. 3.30 P.M., Dr. Critchley: Central Disorders of Vision.
THURSDAY.—2 P.M., Dr. Kinnier Wilson: Out-patient Clinic. 3.30 P.M., Dr. Riddoch: Some Heredo-familial Diseases.
FRIDAY.—12 noon, Dr. Purdon Martin: Anatomy and Physiology of Nervous System. 2 P.M., Dr. Adie: Out-patient Clinic. 3.30 P.M., Mr. Elmquist: Demonstration of Re-educational Methods (in Exercise Room).

NORTH-EAST LONDON POST-GRADUATE COLLEGE, Prince of Wales's General Hospital, Tottenham, N.
MONDAY, Oct. 14th.—2.30 to 5 P.M.: Medical, Surgical, and Gynæcological Clinics. Operations.
TUESDAY.—2.30 to 5 P.M.: Medical, Surgical, Ear, Nose and Throat Clinics. Operations.
WEDNESDAY.—2.30 to 5 P.M.: Medical, Skin, and Eye Clinics. Operations.
THURSDAY.—11.30 A.M.: Dental Clinics. 2.30 to 5 P.M.: Medical, Surgical, Nose, Throat and Ear Clinics. Operations.
FRIDAY.—10.30 A.M.: Throat, Nose and Ear Clinics. 2.30 to 5 P.M.: Surgical, Medical, and Children's Diseases Clinics. Operations.

WEST LONDON HOSPITAL POST-GRADUATE COLLEGE, Hammersmith, W.
MONDAY, Oct. 14th.—10 A.M., Dr. Dowling: Skin Department. 11 A.M., Mr. Tyrrell Gray: Ward Visit. 2 P.M., Mr. Donald Armour: Operations.
TUESDAY.—10 A.M., Medical Registrar: Ward Visit. 2 P.M., Dr. Shaw: Medical Out-patients. 4.30 P.M., (lecture), Mr. Tyrrell Gray: Surgical Aspects of Indigestion.
WEDNESDAY.—10 A.M., Dr. Owen: Children's Out-patient Department. 2 P.M., Mr. Tyrrell Gray: Operations. 2 P.M., Dr. Scott Pinchin: Medical Out-patients.
THURSDAY.—10 A.M., Dr. Grainger Stewart: Neurological Department. 11.30 A.M., Mr. Simmonds: Demonstration of Fractures. 2 P.M., Mr. MacDonald: Genito-Urinary Out-patient Department.
FRIDAY.—10 A.M., Dr. Pritchard: Medical Ward Visit. 12 noon, Dr. Shaw: Clinical Demonstration. 2 P.M., Mr. Vlasto: Throat, Nose and Ear Department.
SATURDAY.—9.30 A.M., Dr. Burnford: Bacterial Therapy Department. 10 A.M., Dr. Owen: Children's Medical Out-patient Department. Medical and Surgical Out-patients at 2 P.M., daily. Operations. Special Departments daily, 10 A.M. to 5 P.M., Saturdays, 10 A.M. to 1 P.M. Special Classes in Anæsthetics and Operative Surgery.

LONDON SCHOOL OF DERMATOLOGY, St. John's Hospital, 49, Leicester-square, W.C.
TUESDAY, Oct. 15th.—5 P.M., Dr. H. W. Barber: Bacteriology and Mycology.
THURSDAY.—5 P.M., Dr. H. G. Burford: Pathology Demonstration.

CENTRAL LONDON THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C.
FRIDAY, Oct. 18th.—4 P.M., Mr. A. Wylie: Gleanings and Impressions of Oto-Rhino-Laryngology.

ST. PAUL'S HOSPITAL, Endell-street, W.C.
WEDNESDAY, Oct. 16th.—4.30 P.M., Mr. R. H. Jocelyn Swan: The Examination of a Urological Patient.

INSTITUTE OF HYGIENE, 28, Portland-place, W.
WEDNESDAY, Oct. 16th.—3.30 P.M., Dr. R. King Brown: Prophylaxis Applied to Infectious Diseases.

ROYAL INSTITUTE OF PUBLIC HEALTH, 37, Russell-square, W.C.
WEDNESDAY, Oct. 16th.—4 P.M., Dr. E. Graham Little, M.P.: Health and Conditions of Work of Medical Students.
FRIDAY.—5 P.M., Prof. R. A. Peters: Coördinative Bio-Chemistry of the Cell and Tissues (First Harben Lecture).

GRESHAM COLLEGE, Basinghall-street, E.C.
TUESDAY, Oct. 15th, and the following Wednesday, Thursday, and Friday.—6 P.M., Sir George Newman: How England Learned to Control Disease (Gresham Lectures).

UNIVERSITY COLLEGE, Gower-street, W.C.
MONDAY, Oct. 14th.—5 P.M., Dr. R. J. Brocklehurst: Secretion of the Digestive Juices. (First of four public lectures).

KING'S COLLEGE, Strand, W.C.
TUESDAY, Oct. 15th.—5 P.M., Mr. J. W. Pickering, D.Sc.: Blood Plasma and Platelets (Second lecture).
THURSDAY.—5 P.M., Mr. J. A. Hewitt, D.Sc.: Metabolism of the Carbohydrates and Fats. (First of four lectures).

ST. THOMAS'S HOSPITAL MEDICAL SCHOOL, Albert Embankment, S.E.
TUESDAY, Oct. 15th.—5 P.M., Dr. A. St. G. Huggett: Physiology of the Fœtus (Second lecture).

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE.
MONDAY, Oct. 14th.—6 P.M., Prof. T. Madsen (Copenhagen): Seasonal Variations of Epidemic Diseases.
WEDNESDAY.—6 P.M., Prof. Madsen: Milk Epidemics.
FRIDAY.—6 P.M., Prof. Madsen: Diphtheria Toxin and Antitoxin.

KING'S COLLEGE FOR HOUSEHOLD AND SOCIAL SCIENCE, Campden Hill-road, W.
FRIDAY, Oct. 18th.—5 P.M., Prof. V. H. Mottram: Human Nutrition (First of six lectures).

MANCHESTER ROYAL INFIRMARY POST-GRADUATE COURSE.
TUESDAY, Oct. 15th.—4.15 P.M., Dr. D. E. Core: Functional Pain.
FRIDAY.—4.15 P.M., Dr. G. Jessel: Differential Diagnosis of Pulmonary Tuberculosis (Illustrated by Skiagrams).

Appointments.

BLIGH, J. M., M.D. Liverp., M.R.C.P. Lond., has been appointed Hon. Consulting Physician to Southport Infirmary.
CHURCHER, D. G., M.D., B.S. Lond., a Medical Referee under the Workmen's Compensation Act for Eastbourne and Hastings County Court Districts.
CLAYE, A. M., M.D. Leeds, F.R.C.S. Eng., Honorary Obstetric Surgeon to Leeds Maternity Hospital.
DEARN, E. M., M.B., Ch.B. Sheffield, Assistant School Medical Officer to the Newcastle Education Committee.
JOHNSON, R. G., Certifying Surgeon under the Factory and Workshop Acts for Bristol District, Gloucester.
LOBBAN, G. M. D., M.B., Ch.B. Leeds, School Medical Officer, Essex County Council.
WATSON, JESSIE R., M.B., Ch.B. St. And., Assistant School Medical Officer, Sunderland.

Bolton Infirmary.—BIGGANE, E. F., M.B., Ch.B. N.U.I., and CRITCHLEY, S. E., M.B., Ch.B. Manch., Assistant Surgeons.

City of London Maternity Hospital, City-road, E.C.—FREEMAN, L. W., L.R.C.P. Lond., M.R.C.S., Resident Medical Officer; and PRICE, J. A., M.B., B.Ch. Belf., Assistant Resident Medical Officer.

Vacancies.

For further information refer to the advertisement columns.

Adelaide University.—Elder Professor of Anatomy and Histology. £1100.

Bath, Royal United Hospital.—H.P. At rate of £120.

Barnstaple Dispensary, Area of the County of Devon.—Tuber. O. £750.

Bedford County Hospital.—H.S. Also Asst. H.S. At rate of £175 and £130 respectively.

Bethlem Hospital, Lambeth-road, S.E.—Res. H.P. £25 per quarter.

Birmingham City Hospital for Infectious Diseases, Little Bromwich.—Temporary Asst. M.O. At rate of £300.

Birmingham, Queen's Hospital.—Res. Anæsthetist. £70–£100.

Birmingham, Selly Oak Hospital.—Cas. O. at rate of £200.

Birmingham and Midland Ear and Throat Hospital.—Asst. Surg. O. £200.

Bolingbroke Hospital, Wandsworth Common, S.W.—H.P. At rate of £120.

Bradford Royal Eye and Ear Hospital.—Jun. H.S. £120.

Bradford Royal Infirmary.—Hon. Asst. P. Also H.P. £150.

Brighton, New Sussex Hospital for Women and Children.—Hon. Asst. Ophth. Surg. Also Hon. Anæsthetist.

Cambridge House Infant Welfare Centre, Camberwell.—M.O. £1 11s. 6d. per session.

Canterbury, Kent and Canterbury Hospital.—Third Res. M.O. At rate of £125.

Carlisle, Cumberland Infirmary.—H.P. At rate of £155.

Chelmsford and Essex Hospital.—Res. M.O. At rate of £150.

Darlington County Borough.—Deputy M.O.H. £750.

Elizabeth Garrett Anderson Hospital, Euston-road, N.W.—Anæsthetist. £10 10s.

Exeter, Royal Devon and Exeter Hospital.—Aural H.S. and Cas. O. At rate of £120.

Glasgow, Woodilee Mental Hospital, Lenzie.—Jun. Asst. M.O. £300.

Great Yarmouth General Hospital.—Jun. H.S. £100.

Halifax Royal Infirmary.—Third H.S. At rate of £100.

Hampstead General and North-West London Hospital, Haverstock Hill, N.W.—H.S. Also Cas. M.O. and Cas. Surg. O. Each at rate of £100.

Hereford General Hospital.—H.P. At rate of £150.

Hospital for Consumption and Diseases of the Chest, Brompton, S.W.—Jun. H.P. for Frimley Sanatorium. At rate of £100.

Hospital for Epilepsy and Paralysis, Maida Vale, W.—Med. Reg. £100. Res. M.O. Also H.P. At rate of £150 and £100 respectively.

Hôpital Français, 172, Shaftesbury-avenue, W.C.—Jun. Res. M.O. £100.

Huddersfield Royal Infirmary.—Jun. H.S. At rate of £150.

Hull Royal Infirmary.—Third H.S. Also Asst. H.P. At rate of £150 and £130 respectively.

Ilford Emergency Hospital.—Hon. Radiologist. £50.

Inverness Northern Infirmary.—Hon. Radiologist.

Lincoln County Hospital.—Jun. H.S. At rate of £150.

Loughboro' Junction Maternity and Infant Welfare Centre, 109, Sussex-road, S.W.—Medical Woman.

Macclesfield General Infirmary.—Second H.S. At rate of £150.

Manchester, St. Mary's Hospital—Four H.S.'s. Each at rate of £50.

Manchester, Baguley Sanatorium.—Sen. Asst. M.O. £500. Also Asst. M.O. £350.

Manchester, Salford Royal Hospital.—H.S. to Orthopædic Dept. Also Cas. H.S. Each at rate of £125.

Margate, Royal Sea Bathing Hospital.—H.S. At rate of £200.

Metropolitan Ear, Nose, and Throat Hospital.—H.S. £150.

Metropolitan Hospital, Kingsland-road, E.—H.P.'s, H.S's., &c. Each at rate of £100.

Mildmay Mission Hospital, Austin-street, Bethnal Green, E.—Jun. Res. M.O. Also Asst. Cas. O. Each at rate of £100.

Miller General Hospital, Greenwich-road, S.E.—Orth. H.S. At rate of £150. Hon. Surgeon. Also Hon. Physician to Skin Dept.

Newcastle-upon-Tyne, Royal Victoria Infirmary.—Hon. Surgeon.

Norwich, Norfolk and Norwich Hospital.—H.P. £120.

Nottingham General Dispensary.—Res. Surg. £250.

Preston and County of Lancaster Royal Infirmary.—Res. Surg. O. £300. Also H.S. At rate of £150.

Prison Medical Service.—Medical Officer. Class II. £350.

Queen's Hospital for Children, Hackney-road, E.—H.P., Cas. O., and H.S. All at rate of £100.

Redhill, Surrey, Royal Earlswood Institution.—Jun. Asst. M.O. At rate of £250.

Rotherham Hospital.—H.P. £180.

Royal Chest Hospital, City-road, E.C.—H.P. At rate of £100.

Royal Eye Hospital, St. George's Circus, Southwark, S.E.—H.S. Also Asst. H.S. At rate of £150 and £100 respectively.

Royal Free Hospital and London (R.F.H.) School of Medicine for Women, W.C.—Obstet. and Gyn. Unit. Sen. Asst. At rate of £350. Third Asst. £270. Path. Dept. Res. Asst. Path. £150.

Royal National Orthopædic Hospital, 234, Great Portland-street, W.—Hon. Asst. Surg. Also Surg. Registrars. Each £105.

Royal Naval Dental Service.—Dental Officers.

Royal Waterloo Hospital for Children and Women, Waterloo-road, S.E.—Hon. Gynæcological Reg. Also H.S. At rate of £100.

St. Andrew's Hospital, Dollis Hill, N.W.—Sen. and Jun. Res. M.O.'s.

St. Helen's County Borough.—Tuber. O. £600.

St. John's Hospital, Lewisham, S.E.—Res. Cas. O. and Res. H.P. Each at rate of £100. Radiologist. Also Res. M.O. At rate of £100.

St. Mary's Hospital, Institute of Pathology and Research.—Research Studentship At rate of £200.

St. Peter's Hospital for Stone, Henrietta-street, W.C.—Radiologist. £25.

Salisbury General Infirmary.—Res. M.O. £150.

Sheffield, South Yorkshire Mental Hospital.—M.O. £400.

Southampton, Royal South Hants and Southampton Hospital.—Cas. O. At rate of £120.

Swanley, Kent, Alexandra Hospital for Children with Hip Disease. Res. Asst. M.O. At rate of £300.

University College Hospital, Gower-street, W.C.—Hon. Clin. Asst.

Victoria Hospital for Children, Tite-street, Chelsea, S.W.—Hon. Med. Reg. Also Hon. Surg. Reg.

West End Hospital for Nervous Diseases, Welbeck-street, W.—Hon. Asst. Physician.

West London Hospital, Hammersmith, W.—Hon. Registrar for Throat, Nose, and Ear Dept. Asst. M.O. At rate of £450. Also three Jun. Asst. M.O's. Each at rate of £350.

Westminster Hospital, Broad Sanctuary.—Wander Scholarship, &c. £250.

Woolwich and District War Memorial Hospital, Shooter's Hill, S.E. Res. M.O. £175. Also H.S. At rate of £125.

Wolverhampton, Royal Hospital.—H.S. Also Cas. O. and Res. Anæsthetist. At rate of £150 and £125 respectively.

The Chief Inspector of Factories announces vacant appointments for Certifying Factory Surgeons at West Hartlepool (Durham) and Montrose (Angus).

Births, Marriages, and Deaths.

BIRTHS.

BEDSON.—On Sept. 29th, at Arkwright-road, Sanderstead, the wife of Dr. S. P. Bedson, of a son.

BUCKLEY.—On Sept. 29th, at Lorna Lodge, Barlow Moor-road, Didsbury, the wife of G. H. Buckley, F.R.C.S. Edin., of Blackpool, of a daughter.

COOPER.—On Sept. 29th, at The Georgian House, Chipstead, the wife of A. Basil Cooper, M.B., of a daughter.

MARRIAGES.

BATCHELOR—GLENDINNING.—On Oct. 1st, at St. Paul's Church, Lorrimore-square, G. F. Grant Batchelor, F.R.C.S., to Louise, daughter of the late Mr. and Mrs. John Glendinning, Dumfries.

MCCAY—DOBBIE.—At Edinburgh, on Oct. 7th, 1929, Andrew William McCay, F.R.C.S.E., Chester, to Elsie Margaret, elder daughter of Sir Joseph and Lady Dobbie, 10, Learmonth-terrace, Edinburgh.

MIDDLETON—LAVANCHY-CLARKE.—On Oct. 2nd, at the Scottish Church, Lausanne, Switzerland, E. L. Middleton, M.D., D.P.H., of London, to Bertha Jane, daughter of the late F. H. Lavanchy-Clarke and of Mrs. Lavanchy-Clarke, of Cannes.

DEATHS.

BROWNFIELD.—On Oct. 5th, Harry Munyard Brownfield, O.B.E., V.D., M.R.C.S., L.R.C.P., of Lennox-road North, Southsea.

FRAKES.—On Sept. 29th, suddenly, at Homecroft, Oakley, Hants, Henry Sowter Frakes, M.D., aged 77.

GORDON.—On Oct. 1st, at Exeter, William Gordon, M.A., M.D. Camb., F.R.C.P. Lond., Consulting Physician to the Royal Devon and Exeter Hospital and West of England, Eye Infirmary, in the 67th year of his age.

O'LEARY.—On Oct. 7th, at Yateley Lodge, Yateley, Hants suddenly, following an operation, Arthur Price Evelyn O'Leary, M.R.C.S., L.R.C.P., late of Gleneig, South Australia, aged 62.

PYWELL.—On Sept. 30th, at Fletton-avenue, Peterborough, Ernest Alfred Pywell, M.R.C.S., L.R.C.P., aged 43.

VERRALL.—On Oct. 4th, at East Lodge, Leatherhead, Sir Thomas Jenner Verrall, M.R.C.S., L.R.C.P., LL.D.

WOODMAN.—At the Royal Hospital, Baghdad, on Sept. 10th, from hæmorrhage during enteric fever, Margaret Maxwell, dearly loved wife of G. S. Woodman, F.R.C.S. Ed.

N.B.—A fee of 7s. 6d is charged for the insertion of Notices of Births, Marriages, and Deaths.

LONDON SCHOOL OF DERMATOLOGY.—The winter session began on Oct. 3rd with an opening lecture on the Rise and Progress of Dermatology delivered by Dr. J. H. Stowers at St. John's Hospital for Diseases of the Skin, Leicester-square. Lectures will be given every Tuesday and Thursday throughout the winter months.

GUILD OF ST. LUKE, ST. COSMAS, AND ST. DAMIAN.—The general meeting of the Guild will be held in the Cathedral Hall, Archbishop's House, on Sunday, Oct. 20th, immediately after the High Mass at Westminster Cathedral, which will be celebrated at 10.30 A.M. The annual report of the council of the Guild records a successful year, special mention being made of the care and helpful direction applied to every activity of the Guild by the Master, Mr. Ernest Ware. The hon. secretary of the Guild is Dr. W. J. O'Donovan, of 123, Harley-street, W.1, from whom further information may be obtained.

Notes, Comments, and Abstracts.

OBSERVATIONS IN ICELAND.

HISTORY AND HEALTH.

(FROM A SPECIAL CORRESPONDENT.)

(*Concluded from p. 750.*)

Other Diseases.

Enteric fever has long been endemic in Iceland, with serious outbreaks from time to time. In the period 1911–20 the annual notifications numbered 155, and in the following five-year period 116. In 1927 only 27 cases were notified. The disease has been most frequent in the towns in spite of a good water-supply, tolerably good drainage, and a standard of cleanliness higher, at any rate, than that of the country districts, where the disease is usually limited to single farms. The disease is often of a mild type, some of the cases being paratyphus. It is most frequent in the first and last quarters of the year. Much of the milk is pasteurised in Reykjavik.

Last century *scarlet fever* invaded the country periodically from abroad, each epidemic running through the country for three or four years, and then dying out completely. Early in the present century it became endemic. The last epidemic, which began in 1909, differed in certain respects from previous epidemics; its maximum was reached in 1920, when there were 700 cases, and it had almost died out by the end of 1924. Its extensive distribution and mild character rendered preventive measures difficult as well as superfluous, and isolation was but little enforced except in Reykjavik. In 1927 only five cases were notified.

Diphtheria was waning in the period 1908–19, but in 1920 a new epidemic wave began, reaching its maximum in 1921, and almost dying out in 1925. In the five-year period 1921–25 there were 201 cases notified annually. In 1926 only 71 cases were notified, mostly mild, and in 1927 this figure was further reduced to 26.

Acute anterior poliomyelitis had been rare in Iceland till 1924, when a serious epidemic broke out suddenly, the first case notified being in Reykjavik. There were 463 cases notified, with 89 deaths, in this year, and in 1925 25 new cases were notified. The epidemic raced through the country in about four months, being most severe in the north and west. As in the case of influenza, this epidemic reached its maximum in its second month. The most remarkable feature of this epidemic was the frequency of abortive cases (two-thirds of all cases according to one medical officer). Another medical officer found 11 abortive cases out of a total of 13. The disease was characterised by a slight sore-throat, nausea or vomiting, and sometimes by diarrhœa, slight fever, headache, and pain or stiffness in the back. Most of the patients recovered rapidly. In some cases the reflexes were a trifle impaired during convalescence from an abortive attack. About half of the members of three families, closely observed during the epidemic, showed some sign of the disease. Patients often had a slight attack without any paralysis at first, but on exertion or exposure a relapse occurred, and this was followed by paralysis. Strict confinement to bed from the onset of symptoms and for a week or two after recovery proved necessary. The proportion of patients who became paralysed varied from 15 to 25 per cent. Twenty-one cases of lethargic encephalitis, with seven deaths, were notified in the five-year period 1921–25.

An epidemic of *whooping-cough* was imported from Denmark in 1926. It raged throughout the country during 1927, as many as 6645 cases being notified, with 155 deaths. As many as 96 of these deaths occurred in the first year of life. Many adults, however, also suffered, several of them catching the disease for a second time. On the other hand, many children proved to be immune, and one medical officer observed that approximately one-third of the children who had been exposed to the disease did not develop it. Some medical officers succeeded by preventive measures in keeping their districts partially or totally free. In Akureyri the advent of the epidemic was greeted by the women of the town in a manner as drastic as it was effective. They formed a cordon round the infected district, and so effective was the day and night watch which the pickets kept that the rest of the town was saved. Preventive vaccination was apparently successful in the hands of several medical officers, and 73·4 per cent. of 168 vaccinated children failed to catch the disease, while 21·6 per cent. caught it only in a mild form. The remaining 5·1 per cent. caught it badly.

In 1922 the Icelandic Medical Society launched a campaign against *favus*, and though only 53 cases were discovered it is probable that this was little more than half the total. With the financial aid of the Government, measures for stamping out the disease were adopted, and in 1925 70 cases were discovered and cured.

Malignant disease is slightly on the increase, but cancer of the uterus still remains remarkably rare. The anatomical distribution of malignant growths notified in Reykjavik was as follows: stomach, 54 per cent.; breast, 14·4 per cent.; œsophagus, 5·8 per cent.; colon, 5·8 per cent.; and uterus, 4·3 per cent.

While *diabetes* is very rare, the rarity of *rickets* is in dispute. In one small district a medical officer, with special training in pædiatrics, found that not less than 18 per cent. of the children under the age of two suffered from this disease. So it may be that rickets in a mild form is not as rare as it was formerly supposed to be, but it is far from being as common as in the Farõe Islands, where 42 per cent. of the children have been found to be rachitic.

Cerebral apoplexy is such a frequent cause of death that in the five-year period 1921–25 there were no fewer than 81 deaths a year from this cause (8·5 per 10,000 inhabitants). This is the more surprising as syphilis is a most rare disease in Iceland. Some curious observations suggest that cerebral apoplexy is an hereditary disease.

Conclusions.

Iceland's public health problems may seem at first sight to be those of any other community, to be solved in the same ways that countries with an older public health service have found to be most satisfactory. But in many respects Iceland is unique, and the features which make it so justify it in adapting, rather than adopting blindly, the ideas and measures of the rest of the world. Take such a matter as the isolation of whole districts when epidemics have reached the country from abroad. As we have seen in the case of measles and influenza, barriers can be raised which are effective, for a time at any rate, against most highly infectious diseases whose very ætiology and mode of dissemination are still largely unknown. Even when such preventive measures have proved of only temporary value the results have merited the careful study of epidemiologists elsewhere.

In such an isolated and sparsely populated country an invading germ can be followed almost visually, as it passes from one lone farmstead to another, and it is subject to an attention as disconcerting and personal as that which would be bestowed on a foreign burglar misguided enough to choose Iceland for his field of operations. So much for the geographical character of the country which makes it so helpfully transparent in the eyes of the epidemiologist. It is transparent in another sense. In the crowded, patchwork civilisations of other countries it is a wise man who knows his own father, and a clairvoyant who knows his own grandfathers. But in Iceland everyone can follow his ancestry back a thousand years. Think what this must mean to the student of the problems of heredity! The country is transparent not only geographically and contemporaneously but also historically.

Iceland's comparative isolation for 1000 years has provided a vast mass of material for the study of environment as well as of heredity. The sheep brought over by the early Norwegian settlers differ in certain respects from the sheep in Norway to-day, and it is possible that the descendants of the settlers themselves have developed on lines not altogether identical with those followed on the Scandinavian mainland. Here again there is a very interesting field of study awaiting the anthropologist. Prof. Hannesson's anthropological studies have already blazed a track in this hitherto almost unexplored sphere.

There are many striking differences in the behaviour of certain diseases in Iceland and other countries. A study of these differences might well throw important light on the ætiology of these diseases. It is easy enough to understand why the bacillus of leprosy and the ecchinococcus should have been comparatively common in Iceland up to the end of the last century. But the country's remarkable immunity to certain other diseases, which are relatively common elsewhere, is to a large extent an unsolved problem. Why should acute rheumatism run so mild a course and the cardiac complications thereof be so infrequent? Why should diabetes be almost unknown, and cancer of the uterus so rare? Why should cerebral apoplexy be so common in the almost complete absence of syphilis? Why should this accident apparently run in families? The prospect of answers being found to these and other questions is enhanced by the high standard of the medical profession in Iceland and by its intimate and steadily growing contact with medical science abroad. Were this contact to be promoted by every possible means I am sure that the

accruing benefit would not be one-sided. Iceland should prove a happy hunting ground for research workers, not only for the reasons already given, but also because the Icelandic medical profession receives the medical stranger within its gates with a most charming and spontaneous hospitality.

My most grateful thanks are due to Prof. Gudmundur Thoroddsen, Dr. Olafur O. Larusson, of the Vestmanöy Islands, and Dr. Gunnlaugur Claessen for the help they gave me.

THE EFFECT OF TOXÆMIA ON THE FORMATION OF ENAMEL.

HYPOPLASIA of the dental enamel, characterised by a honeycombed or pitted condition of this tissue, is comparatively common. It has long been recognised that it is often due to some disease or metabolic disturbance during the period of calcification, the subsequent eruption of the affected teeth remaining a permanent record of a past defect in nutrition. Hypoplastic teeth are still sometimes termed rachitic teeth on the supposition that rickets is the chief disease resulting in enamel defect. We know now that while rickets often brings about defective calcification, other diseases also, especially the infective diseases of childhood, may leave their mark on the teeth. Since the dates of calcification are known, the observer can usually predict with tolerable accuracy the times when the disturbance in nutrition affected the portion of the enamel defectively formed.

Dr. L. B. Stott and Mr. W. B. Grandison have investigated the occurrence of dental hypoplasia in children at the Papworth Village Settlement, and their results have been published in an attractively produced monograph.[1] They have been struck by the fact that during dental inspection of the children at this Settlement some showed perfect dentitions, while their general condition and personal hygiene did not differ from that of sufferers from varying degrees of dental caries. This has led them to examine the dental and medical records with a view to ascertaining the significance of this apparent immunity from dental disease. The correlation of the medical and dental records leads them to the view that infective disease during calcification produces hypoplasia while, as a necessary corollary to this, they suggest that acquired resistance to infectious disease is followed by satisfactory calcification.

The interesting suggestion is made that the calcium metabolism in the teeth follows those variations in the calcium metabolism of the body as a whole which occur in active tuberculosis and its arrest. In active tubercle the calcium excretion is high, so the teeth in process of calcification do not receive enough lime salts and are therefore defectively formed. When tuberculosis is arrested the process is characterised by the deposition of calcium in the tuberculous foci. Thus deposition of calcium is a tissue action which may be widespread in and is associated with a low calcium excretion. Hence it might follow that in cases of acquired immunity the teeth undergoing calcification receive plenty of calcium and are, in consequence, highly calcified and resistant to caries.

A further point of some theoretical importance raised by Stott and Grandison is whether this power of depositing calcium is part of a natural resistance or whether it is increased by exposure to infection and is thus due to acquired immunity. They suggest—though they do not bring much evidence to support the suggestion—that efficient calcification is conferred by acquired rather than natural immunity. This seems to mean that the dental enamel is more highly calcified in children who have been exposed to infection, which they have subsequently overcome successfully, than in children who have escaped exposure to infection altogether. The logical and somewhat surprising outcome is that immunity to dental caries, instead of being a function of a normal calcium metabolism leading to normally formed enamel, is rather a function of an abnormal calcium metabolism which causes excessive calcification of the enamel.

THE FUTURE OF MONOGAMY.

A PROPHECY that the years 1930 to 1975 will be a period of sexual reform, during which the institution of monogamy will undergo vicissitudes consequent upon the universal teaching of sex hygiene and the liberation of marriage from external inhibitions, is made in an addition to the To-day and To-morrow Series, which has reached us.[2] The period 2000 to 2030, however, will see the triumph of voluntary monogamy. The somewhat startling reason for this is that "no type of union has yet been discovered in which the maximum of intellectual variety may be so effectually combined with the minimum of emotional disturbance." The book is written in the form of a chapter out of a hypothetical history of moral institutions in the nineteenth, twentieth, and twenty-first centuries. The contemporary literature on which the survey is based is not representative, the chief sources being the series in which this book appears. In the course of the next hundred years, the author thinks, the institution of monogamy will have completed a circle, ending up much as it is now, except that it will be voluntary instead of compulsory, and based on sexual knowledge instead of upon ignorance. The psychological presupposition of this desirable change is that confidence will be gained in humanity's ability to impose voluntary restraints upon its conduct. No attempt whatever is made to analyse the growth of these morally inhibiting processes, and the relevant psychological literature is nowhere referred to.

MEDICAL MISSIONS.

A LITTLE book called "The Touch of Healing," by M. M. Wood,[1] will be welcomed by anyone who wishes to give young people a vivid description of medical missionary work. It is attractively written and illustrated, and is full of arresting anecdotes, drawn from every corner of the world where missionary work is carried on. The photographs come from India, China, Egypt, and Palestine. The training and work of a missionary nurse is sketched out, and the treatment—often in bulk—of all kinds of tropical disease is described. The value of medical missions is undisputed, and the tales in this book show how western science is appreciated by the races to whom it is taken by these devoted men and women.

CASH BEFORE NON-DELIVERY.

M. R. D. (Wembley) has received a call from a man desirous of obtaining orders for printing, corks, bottles, and the like, who presents as his credential the card of a professional colleague. After receiving payment in advance, nothing more is heard of him. Obviously any instances of frauds of this nature should be promptly reported to the police, in order to teach a lesson to the unscrupulous persons who seek to victimise medical practitioners. The number of these is large, partly because they can so easily obtain an interview, partly, one fears, because practitioners are regarded as readily imposed upon. We would once again warn members of the medical profession to be on their guard against dealing with persons who are entirely unknown to them, with a special caution against making cash payments for goods prior to delivery.

A NURSE'S SALARY DURING ILLNESS.

A. L. M.—The payment of salary during the illness of a nurse is a matter of usage rather than of obligation. The usual practice, both in institutions and on the district, is to pay full salary during sickness for a period dependent upon the length of service the nurse has rendered. Most institutions would retain her national insurance benefit, but some district nursing associations allow a nurse who has been in their service for some time, and who is not well off financially, to retain her benefit for a period. One well-known nursing institute is considering the equity of recommending full salary and allowance for board for six weeks, and after that half the amount. The private nurse must, unfortunately, make her own provision for sickness: but hospitals will often give her free accommodation and care.

DANGEROUS DRUG RECORDS.

H. E. S.—A duly qualified medical practitioner is "authorised" to be in possession of dangerous drugs and to apply them by personal administration. In purchasing the drugs he is subject to the conditions of the Pharmacy Acts relating to the sale of poisons—e.g., signing the poison-book, and so forth. If the practitioner requires the drugs solely for administration to his patients by himself personally, or under his own direct supervision, he is under no obligation to keep the records required by the Regulations in the case of dispensing doctors. If, on the other hand, he dispenses or supplies medicine (which the Home Office interprets as including the case of a doctor leaving a supply of any of the drugs with a nurse for administration to a patient during the doctor's absence), he must keep the prescribed registers.

THE British Social Hygiene Council would be glad to hear from medical men and women willing to give single lectures in London or to undertake short campaigns in the provinces. The fee for a single lecture in London is 1 guinea. Application to the Secretary-General of the Council, Carteret House, Carteret-street, London, S.W. 1.

[1] An Investigation into the Effect of Toxæmia on Enamel Formation. By L. B. Stott, M.B., and W. Baird Grandison, L.D.S. With a Foreword by Sir Humphry Rolleston. From the Dental Unit of the Papworth Village Settlement, 1929.

[2] Halcyon, or the Future of Monogany. By Vera Brittain. London: Kegan Paul, Trench, Trubner and Co. 1929. Pp. 92. 2*s*. 6*d*.

[1] Edinburgh House Press, 2, Eaton-gate, S.W. Pp. 62. 1*s*.